ONCOLOGY DRUG UPDATES

ONCOLOGY THERAPEUTICS NETWORK

Temozolomide ('Temodal', Schering), A New Agent for Brain Tumors

Jane Pruemer Pharm.D.

Temozolomide is a new oral antineoplastic agent that recently received an Oncology Drugs Advisory Committee (ODAC) recommendation for Food and Drug Administration approval for the treatment of anaplastic astrocytomas. Temozolomide, a pro-drug originally synthesized in the 1960s, is a triazene that under physiologic conditions, undergoes ring-opening to the monomethyltriazene (MTIC) ring, the active form of the drug. Unlike dacarbazine (DTIC), MTIC achieves adequate penetration through the blood-brain barrier, facilitating management of various brain tumors. Although the precise mechanism of action of temozolomide has yet to be defined, a methylation reaction at the O^6 position of the guanine residue probably occurs.[1] Reports indicate that up to 22% of primary brain tumors have no detectable levels of the repair enzyme methyltransferase. Therefore, these brain tumors cannot correct the damage caused by temozolomide. With temozolamide, clinical activity has been observed in the treatment of melanoma, astrocytomas, and mycosis fungoides.

In early clinical trials, temozolomide 50 to 200 mg/m² was administered intravenously as a single dose. It is stable at an acidic pH, allowing it to be absorbed intact after oral administration. After the development of the oral formulation, doses of 200 to1,200 mg/m² were administered in additional trials. Temozolomide's area under the curve (AUC) is linear based on the dose administered, and its activity is highly schedule dependent. In recent clinical trials, the drug has been administered for five days every four weeks, in an attempt to optimize temozolomide's schedule-dependent effect.

At single oral doses of 1 g/m², temozolomide's dose-limiting toxicity is myelosuppression. Myelosuppression may also be observed when temozolomide treatment is combined with extensive field radiation therapy or in patients with prior nitrosourea treatment. Additionally nausea and vomiting may occur, particularly with higher doses. Alopecia is uncommon with this agent.

Temozolomide in Gliomas

The Charing Cross Hospital in London reported one of the first trials of temozolomide in the treatment of patients with gliomas.[2] Seventy-five patients with malignant primary gliomas received temozolomide at an initial dosage of 150 mg/m²/d for five days (total dose, 750 mg/m²), which was escalated to 200 mg/m²/d for five days if significant myelosuppression did not occur. Subsequent cycles were administered every four weeks. Of the 75 patients eligible to receive temozolomide, 48 had recurrent disease following radiation therapy; 27 patients had newly diagnosed gliomas and were treated following their initial surgery and before cranial irradiation. Results of the trial were as follows: In the patients with recurrent disease, an objective response rate of 25% occurred in 12 patients, and 18 patients (38%) experienced stable disease. Patients with newly diagnosed disease achieved a higher objective response rate (30%), as well as a higher rate of stable disease (48%). The performance status in the patients with newly diagnosed disease was better than in patients with recurrent disease. In addition, the newly diagnosed patients received cranial radiation therapy following temozolomide treatment, which may have contributed to the increased overall response. The overall one-year survival rate in patients with new diagnoses was 43%, compared with 22% in patients with recurrent disease who were subsequently treated with temozolomide.

Temozolomide in Metastatic Melanoma

A phase II trial evaluated temozolomide in chemotherapy-naive patients with metastatic melanoma.[3] Sixty patients with measurable advanced malignant melonoma received oral temozolomide 150 mg/m²/d on days one to five, every four weeks. The dosage was escalated to 200 mg/m²/d for five days if toxicity was acceptable after the first course. Fifty-five patients were

Continued on next page

References

1. Tsany LL, Quarterman CP, Gescher A, Slack JA. Comparison of the cytotoxicity in vitro of temozolomide and dacarbazine, prodrugs of 3-methyl-triazen-1-yl)imidazole-4-carboxamide. *Cancer Chemother Pharmacol.* 1991;27:342-346.
2. Newlands ES, O'Reilly SM, Glaser MG, et al. The Charing Cross Hospital experience with temozolomide in patients with gliomas. *Eur J Cancer.* 1996;32A:2236-2241.
3. Bleehen NM, Newlands ES, Lee SM, et al. Cancer research campaign Phase II trial of temozolomide in metastatic melanoma. *J Clin Oncol.* 1995;13:910-913.
4. Nicholson HS, Krailo M, Ames MM, et al. Phase I study of temozolomide in children and adolescents with recurrent solid tumors: a report from the Children's Cancer Study Group. *J Clin Oncol.* 1998;16:3037-3043.
5. Raymond E, Isbick E, Soda H, et al. Activity of temozolomide against human tumor colony-forming units. *Clin Cancer Res.* 1997;3:1769-1774.
6. Spagnolli F, Boni C, Gagliardi R, et al. Activity of temozolomide in recurrent malignant gliomas: a phase II study. *Pro Amer Soc Clin Oncol.* 1999;18:A590.
7. Stupp R, Maillard I, Fico A, et al. Daily temozolomide (TMZ) and concomitant radiotherapy followed by adjuvant TMZ for newly diagnosed glioblastoma multiforme. A well tolerated and promising regimen. *Pro Amer Soc Clin Oncol.* 1999;18:A592.
8. Yung A, Levin VA, Albright R, et al. Randomized trial of temodal vs. procarbazine in glioblastoma multiforme at first relapse. *Pro Amer Soc Clin Oncol.* 1999;18:A532.

assessable for toxicity and 49 for response. A complete response was documented in three patients (lung metastases) and a partial response in nine patients, for an overall response rate of 21%. Hematologic toxicity, although primarily low grade, was reported. Treatment was delayed in two patients because of thrombocytopenia, and in one patient each because of leukopenia and gastrointestinal upset. The authors concluded that temozolomide has good activity in chemotherapy-naive patients with metastatic melanoma and that further studies of temozolomide, both as a single agent and in combination with other antineoplastic agents, are warranted.

Temozolomide in Various Solid Tumors

In studies of children with various solid tumors, temozolomide has been found to be well tolerated.[4] The Children's Cancer Study Group conducted a phase I trial of temozolomide in 27 patients, the results of which indicated that the maximally tolerated dose for children without prior craniospinal irradiation is 215 mg/m^2 and for children without prior irradiation of the brain and cord 180 mg/m^2. Additional phase II trials of children are ongoing.

Conclusions

The side effects of temozolomide are primarily to the bone marrow and to the gastrointestinal tract. Myelosuppression is the dose-limiting toxicity, with neutropenia and thrombocytopenia predominating. The bone marrow effect is accentuated by the concomitant administration of radiation therapy. The degree of marrow suppression is dependent upon prior chemotherapy administration, and in a clinical trial of recurrent malignant gliomas, only one patient of 21 experienced grade 3 thrombocytopenia, despite previous treatment with chemotherapy.[6] Gastrointestinal effects are primarily low grade nausea. Other reported side effects include lymphopenia, infections, seizures, fatigue, and anxiety.[7]

Several clinical trials of temozolomide were presented at the recent American Society of Clinical Oncology meeting in Atlanta. With regard to its use in the treatment of glioblastoma multiforme (GBM), the agent appeared to provide a significantly better progression-free survival than procarbazine, and patients treated with temozolomide also had a longer survival and better overall quality of life.[8] Published abstracts of temozolomide use for the treatment of newly diagnosed GBM with concomitant radiotherapy have indicated that the drug is safe to use as part of a combined modality approach.[7]

Temozolomide, an agent that demonstrates rapid oral absorption and high systemic availability, has demonstrated activity in malignant gliomas, metastatic melanoma, and a variety of other tumors, including mycosis fungoides. Cell culture data indicate good cytotoxic activity in cell lines, including breast, ovarian, and non–small-cell lung cancers.[5] Temozolomide will soon be available for oral use in the treatment of brain tumors, and this agent continues to be studied in clinical trials.

ODAC Recommendations

The Oncologic Drugs Advisory Committee (ODAC) has recommended the approval of temozolomide (Temodal™, Schering) for the treatment of adult patients with anaplastic astrocytoma who have relapsed following prior therapy with a nitrosourea and procarbazine. This oral imidazotetrazine acts as an alkylating agent, its primary toxicity being myelosuppression. Although ODAC voted not to recommend temozolomide for the treatment of adult patients with glioblastoma multiforme, the manufacturer, Schering-Plough, continues to study the agent in this more aggressive form of primary brain cancer.

ONCOLOGY THERAPEUTICS NETWORK

Average Wholesale Prices and 1999 HCPCS Codes

The Average Wholesale Prices (AWPs) and HCPCS codes for drugs commonly used in cancer treatment are provided for your use as a reimbursement resource. Products are listed alphabetically by their generic name. The AWPs are obtained from the *1999 Red Book* and the *June 1999 Red Book Update*.

For drugs that have multiple manufacturers, the AWP for the product most commonly stocked by OTN is listed. For ease of use, we list the AWP information in the first three columns and the billing code and units in the two right columns. Please refer to the *Sourcebook* for a complete listing of HCPCS codes.

PRODUCT	VIAL SIZE	NDC	JUNE AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Proleukin®					
Aldesleukin, pwd (Interleukin-2)	22 MIU	53905-0991-01	557.50	J9015	per 22 MIU
Ethyol®					
• Amifostine	500 mg	17314-7253-03	368.75	J0207	per 500 mg
Fungizone®					
Amphotericin B Oral Suspension	24 mL	00087-1162-10	26.25	J9999*/J3490*	
Blenoxane®					
Bleomycin sulfate, pwd	15 units	00015-3010-20	304.60	J9040	per 15 units
	30 units	00015-3063-01	609.20	J9040	per 15 units
Xeloda®					
• Capecitabine	150 mg	00004-1100-51	237.52		
•	500 mg	00004-1101-16	1,583.40		
Paraplatin®					
• Carboplatin, pwd	50 mg	00015-3213-30	104.11	J9045	per 50 mg
•	150 mg	00015-3214-30	312.30	J9045	per 50 mg
•	450 mg	00015-3215-30	936.90	J9045	per 50 mg
BiCNU®					
• Carmustine, pwd w/diluent	100 mg	00015-3012-38	103.54	J9050	per 100 mg
Tagamet®					
Cimetidine HCl, sol (150 mg/mL)	300 mg	00108-5017-16	3.96	J9999*/J3490*	
Platinol®-AQ					
• Cisplatin, sol (1 mg/mL)	50 mg MDV	00015-3220-22	221.44	J9062	per 50 mg
•	100 mg MDV	00015-3221-22	442.85	J9062	per 50 mg
Leustatin®					
Cladribine, sol (1 mg/mL)	10 mg	59676-0201-01	541.28	J9065	per 1 mg
Cytogam®					
• Cytomegalovirus immunoglobulin intravenous, human	50 mL	60574-3101-01	644.41	J0850	per vial
Cytoxan® lyophilized					
Cyclophosphamide, lyophilized	100 mg	00015-0539-41	6.45	J9093	per 100 mg
	200 mg	00015-0546-41	12.25	J9094	per 200 mg
	500 mg	00015-0547-41	25.71	J9095	per 500 mg
	1 g	00015-0548-41	51.43	J9096	per 1 g
	2 g	00015-0549-41	102.89	J9097	per 2 g
Cytoxan® Tablets					
• Cyclophosphamide, tablets, 25 mg	100 per bottle	00015-0504-01	212.34	J8530	25 mg
• Cyclophosphamide, tablets, 50 mg	100 per bottle	00015-0503-01	389.68	J8530	25 mg
• Cyclophosphamide, tablets, 50 mg	1,000 per bottle	00015-0503-02	3,711.44	J8530	25 mg
Cytarabine, pwd	100 mg	55390-0131-10	6.25	J9100	per 100 mg
	500 mg	55390-0132-10	25.00	J9110	per 500 mg
	1 g	55390-0133-01	50.00	J9110	per 500 mg
	2 g	55390-0134-01	98.90	J9110	per 500 mg
DTIC-Dome®					
Dacarbazine, pwd	100 mg	00026-8151-10	13.83	J9130	per 100 mg
	200 mg	00026-8151-20	22.23	J9140	per 200 mg
DaunoXome®					
• Daunorubicin citrate liposome inj. (1 mg/mL)	50 mg	56146-0301-01	340.00	J9999*/J3490*	per 10 mg
Cerubidine®					
Daunorubicin HCl, pwd	20 mg	55390-0281-10	168.50	J9150	per 10 mg
DDAVP®					
Desmopressin Acetate, sol (4 mcg/mL)	1 mL	00075-2451-01	26.69	J2597	per 4 mcg
Dexamethasone, sol (4 mg/mL)	20 mg MDV	00517-4905-25	2.19	J1100	up to 4 mg/mL
	120 mg MDV	00517-4930-25	7.84	J1100	up to 4 mg/mL
Zinecard®					
Dexrazoxane for injection	250 mg	00013-8715-62	158.49	J1190	per 250 mg
	500 mg	00013-8725-89	316.95	J1190	per 250 mg
• Diphenhydramine HCl, sol (50 mg/1 mL)	50 mg	00641-0376-25	.69	J1200	
Taxotere®					
Docetaxel for injection	20 mg	00075-8001-20	284.36	J9170	per 20 mg
	80 mg	00075-8001-80	1,137.43	J9170	per 20 mg
Anzemet®					
Dolasetron mesylate, sol (20 mg/mL)	5 mL	00088-1206-3	155.88	J1260	per 1 mg
Rubex®					
Doxorubicin, pwd	50 mg	00015-3352-22	197.15	J9000	per 10 mg
	100 mg	00015-3353-22	394.29	J9000	per 10 mg

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	JUNE AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Bedford Laboratories					
Doxorubicin, pwd	10 mg	55390-0231-10	45.08	J9000	per 10 mg
	20 mg	55390-0232-10	90.16	J9000	per 10 mg
	50 mg	55390-0233-01	225.40	J9000	per 10 mg
Doxorubicin, sol (2 mg/mL)	10 mg	55390-0235-10	47.35	J9000	per 10 mg
	20 mg	55390-0236-10	94.70	J9000	per 10 mg
	50 mg	55390-0237-01	236.74	J9000	per 10 mg
	200 mg MDV	55390-0238-01	945.98	J9000	per 10 mg
Adriamycin™					
Doxorubicin, RDF pwd	10 mg	00013-1086-91	53.64	J9000	per 10 mg
	20 mg	00013-1096-94	92.00	J9000	per 10 mg
	50 mg	00013-1106-79	268.18	J9000	per 10 mg
	150 mg MDV	00013-1116-83	788.49	J9000	per 10 mg
Doxorubicin, pfs sol (2 mg/mL)	10 mg	00013-1136-91	56.34	J9000	per 10 mg
	20 mg	00013-1146-94	112.66	J9000	per 10 mg
	50 mg	00013-1156-79	281.68	J9000	per 10 mg
	75 mg	00013-1176-87	422.51	J9000	per 10 mg
	200 mg MDV	00013-1166-83	1,104.13	J9000	per 10 mg
DOXIL®					
Doxorubicin, HCl liposome inj. (2mg/mL)	20 mg	61471-0295-12	656.25	J9999*	
Procrit®					
Epoetin alfa	2,000 units/ mL	59676-0302-01	24.00	Q0136*	1,000 units
	3,000 units/ mL	59676-0303-01	36.00	Q0136*	1,000 units
	4,000 units/ mL	59676-0304-01	48.00	Q0136*	1,000 units
	10,000 units/ mL	59676-0310-01	120.00	Q0136*	1,000 units
	20,000 units/ 1 mL MDV	59676-0320-01	240.00	Q0136*	1,000 units
	40,000 units/ 1 mL SDV	59676-0340-01	480.00	Q0136*	1,000 units
VePesid® *Capsules*					
Etoposide, capsules, 50 mg	20 per box	00015-3091-45	751.60	J8560	50 mg
VePesid® *For Injection*					
Etoposide, injection (20 mg/mL)	100 mg MDV	00015-3095-20	136.49	J9182	per 100 mg
	150 mg MDV	00015-3084-20	204.74	J9182	per 100 mg
	500 mg MDV	00015-3061-20	665.38	J9182	per 100 mg
	1 gm MDV	00015-3062-20	1,296.64	J9182	per 100 mg
Etopophos®					
Etoposide phosphate for injection	100 mg	00015-3404-20	124.14	J9999*	per 100 mg
Fludara®					
Fludarabine phosphate, pwd	50 mg	50419-0511-06	228.56	J9185	per 50 mg
Fluorouracil, sol (50 mg/mL)	500 mg	39769-1036-91	3.20	J9190	per 500 mg
	2,500 mg	00013-1046-94	16.04	J9190	per 500 mg
	5,000 mg	39769-1056-94	32.06	J9190	per 500 mg
Neupogen®					
G-CSF (Filgrastim), sol (0.3 mg/mL)	300 mcg	55513-0530-10	172.30	J1440	per 300 mcg
	480 mcg	55513-0546-10	274.40	J1441	per 480 mcg
Gemzar®					
• Gemcitabine HCl	200 mg	00002-7501-01	93.12	J9201	per 200 mg
•	1 g	00002-7502-01	465.59	J9201	per 200 mg
Leukine®					
GM-CSF (Sargramostim), lyophilized	250 mcg	58406-0002-33	134.85	J2820	per 50 mcg
• Leukine Liquid® (Sargramostim), solution	500 mcg	58406-0001-35	252.06	J2820	per 50 mcg
Zoladex®					
Goserelin acetate, implant	3.6 mg syringe	00310-0960-36	469.99	J9202	per 3.6 mg
	10.8 mg syringe	00310-0961-30	1,409.98	J9202	per 3.6 mg
Kytril®					
• Granisetron HCl, sol (1 mg/mL)	1 mL	00029-4149-01	186.10	J1626	per 100 mcg
•	4 mL	00029-4152-01	744.35	J1626	per 100 mcg
Ifex®					
• Ifosfamide	1 g	00015-0556-41	141.76	J9208	per 1 g
•	3 g	00015-0557-41	425.29	J9208	per 1 g
Ifex®/*Mesnex*™					
• Ifosfamide (10 x 1 g)/mesna (10 x 1 g MDV)	Combo-Pack	00015-3554-27	2,356.28	J9208/J9209	
• Ifosfamide (2 x 3 g)/mesna (6 x 1 g MDV)	Combo-Pack	00015-3564-15	1,413.70	J9208/J9209	
• Ifosfamide (5 x 1 g)/mesna (3 x 1 g MDV)	Combo-Pack	00015-3556-26	975.14	J9208/J9209	
Venoglobulin I					
Immunoglobulin intravenous, 5% pwd w/V set	2.5 g	49669-1602-01	152.05	J1561	per 500 mg
	5 g	49669-1603-01	304.10	J1561	per 500 mg
	10 g	49669-1604-01	608.20	J1561	per 500 mg
Venoglobulin S					
Immunoglobulin intravenous, 5% sol w/V set	2.5 g	49669-1612-01	225.00	J1561	per 500 mg
	5 g	49669-1613-01	450.00	J1561	per 500 mg
	10 g	49669-1614-01	900.00	J1561	per 500 mg
Immunoglobulin intravenous, 10% sol w/V set	5 g	49669-1622-01	475.00	J1562	per 5 g
	10 g	49669-1623-01	950.00	J1562	per 5 g
	20 g	49669-1624-01	1,900.00	J1562	per 5 g

REIMBURSEMENT

ONCOLOGY THERAPEUTICS NETWORK

PRODUCT	VIAL SIZE	NDC	JUNE AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Immunoglobulin intravenous 10% sol w/V set	1 g	00192-0649-12	75.00	J1561	per 500 mg
	5 g	00192-0649-20	375.00	J1562	per 5 g
	10 g	00192-0649-71	750.00	J1562	per 5 g
	20 g	00192-0649-24	1,500.00	J1562	per 5 g
	1 g	00026-0648-12	90.00		
	5 g	00026-0648-20	450.00		
	10 g	00026-0648-71	900.00		
	20 g	00026-0648-24	1,800.00		
Immunoglobulin intravenous 5%-10% w/V set	2.5 g	52769-0471-72	168.93	J1561 or J1562	
	5 g	52769-0471-75	337.86	J1561 or J1562	
	10 g	52769-0471-80	675.72	J1561 or J1562	
RhoD Immunoglobulin intravenous	120 mcg	60492-0021-01	142.00	J2792	
	300 mcg	60492-0023-01	324.50	J2792	
	1,000 mcg	60492-0024-01	1,081.50	J2792	
Intron® A					
• Interferon alfa-2b, solution HSA-free	3 MIU	00085-1184-01	35.63	J9214	per 1 MIU
•	3 MIU PAK	00085-1184-02	35.63	J9214	per 1 MIU
•	5 MIU	00085-1191-01	59.38	J9214	per 1 MIU
•	5 MIU PAK	00085-1191-02	59.38	J9214	per 1 MIU
•	10 MIU	00085-1179-01	118.76	J9214	per 1 MIU
•	10 MIU PAK	00085-1179-02	118.76	J9214	per 1 MIU
•	18 MIU MDV	00085-1168-01	213.77	J9214	per 1 MIU
•	25 MIU MDV	00085-1133-01	296.93	J9214	per 1 MIU
• Interferon alfa-2b, pwd	3 MIU MDV	00085-0647-03	35.63	J9214	per 1 MIU
•	5 MIU MDV	00085-0120-02	59.38	J9214	per 1 MIU
•	10 MIU MDV	00085-0571-02	118.76	J9214	per 1 MIU
•	18 MIU MDV	00085-1110-01	213.77	J9214	per 1 MIU
•	25 MIU MDV	00085-0285-02	296.93	J9214	per 1 MIU
•	50 MIU MDV	00085-0539-01	593.81	J9214	per 1 MIU
Roferon® A					
Interferon alfa 2a, pwd w/3 mL diluent	18 MIU	00004-1993-09	197.56	J9213	per 3 MIU
Interferon alfa 2a, sol (3 MIU/mL)	3 MIU	00004-2009-09	34.97	J9213	per 3 MIU
Interferon alfa 2a, sol (6 MIU/mL)	6 MIU	00004-2007-09	69.91	J9213	per 3 MIU
Interferon alfa 2a, sol (10 MIU/mL)	9 MIU	00004-2010-09	98.44	J9213	per 3 MIU
Interferon alfa 2a, sol (6 MIU/mL)	18 MIU	00004-2011-09	209.60	J9213	per 3 MIU
Interferon alfa 2a, sol (36 MIU/mL)	36 MIU	00004-2012-09	419.26	J9213	per 3 MIU
Camptosar®					
Irinotecan HCl injection, CPT-11 (20 mg/mL)	2 mL	00009-7529-02	231.80	J9206	per 20 mg
	5 mL	00009-7529-01	579.53	J9206	per 20 mg
Leucovorin, pwd	50 mg	55390-0051-10	18.44	J0640	per 50 mg
	50 mg	58406-0621-05	21.53	J0640	per 50 mg
	100 mg	55390-0052-10	35.00	J0640	per 50 mg
	100 mg	58406-0622-06	39.41	J0640	per 50 mg
	200 mg	55390-0053-01	78.00	J0640	per 50 mg
	350 mg	58406-0623-07	137.94	J0640	per 50 mg
Lupron®					
Leuprolide acetate depot, susp. (7.5 mg/mL)	7.5 mg	00300-3629-01	594.65	J9217	per 7.5 mg
	22.5 mg	00300-3346-01	1,783.95	J9217	per 7.5 mg
Lorazepam, sol (2 mg/mL)	2 mg MDV	00008-0581-04	9.85	J2060	per 2 mg
Lorazepam, sol (2 mg/mL)	20 mg MDV	00008-0581-01	87.74	J2060	per 2 mg
Lorazepam, sol (4 mg/mL)	40 mg MDV	00008-0570-01	109.66	J2060	per 2 mg
Lorazepam, sol (2 mg/mL), w/ syringe	2 mg	00008-0581-02	10.39	J2060	per 2 mg
Mannitol, 25% sol	50 mL	00074-4031-01	5.29	J2150	per 50 mL
Mustargen®					
Mechlorethamine HCl, pwd	10 mg	00006-7753-31	10.48	J9230	per 10 mg
Megace®					
Megestrol acetate, tablets, 20 mg	100 per bottle	00015-0595-01	75.68		
Megestrol acetate, tablets, 40 mg	100 per bottle	00015-0596-41	134.96		
	250 per bottle	00015-0596-46	330.68		
	500 per bottle	00015-0596-45	647.88		
Megace® Oral Suspension					
Megestrol acetate, oral suspension	8 fl oz	00015-0508-42	131.96		
Alkeran®					
Melphalan hydrochloride, pwd	50 mg	00173-0130-93	364.74	J9245	per 50 mg
Melphalan hydrochloride, tablets, 2 mg	50 per bottle	00173-0045-35	104.11	J8600	2 mg
Mesnex™					
Mesna, sol (100 mg/mL)	1 g MDV	00015-3563-02	174.30	J9209	per 200 mg
Methotrexate, pwd	20 mg	00205-4654-90	2.78	J9250	per 5 mg
	20 mg	58406-0673-01	5.03	J9250	per 5 mg
	1,000 mg	58406-0671-05	61.44	J9260	per 50 mg
Methotrexate, pres. free sol (25 mg/mL)	50 mg	55390-0031-10	6.88	J9260	per 50 mg
	100 mg	55390-0032-10	8.75	J9260	per 50 mg
	200 mg	55390-0033-10	17.50	J9260	per 50 mg
	250 mg	55390-0034-10	26.88	J9260	per 50 mg
Methotrexate, sol w/pres. (25 mg/mL)	50 mg	58406-0681-14	4.75	J9260	per 50 mg
	250 mg	58406-0681-17	20.48	J9260	per 50 mg
Methotrexate, tablets, 2.5 mg	100 per bottle	00555-0572-02	362.95	J8610	2.5 mg
	36 per bottle	00555-0572-35	130.05	J8610	2.5 mg

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	JUNE AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Metoclopramide, pres. free sol (5 mg/mL)	50 mg	00013-6116-95	8.73	J2765	up to 10 mg
	150 mg	00013-6126-95	23.54	J2765	up to 10 mg
Mutamycin®					
Mitomycin, pwd	5 mg	00015-3001-20	134.11	J9280	per 5 mg
	20 mg	00015-3002-20	452.91	J9290	per 20 mg
	40 mg	00015-3059-20	915.09	J9291	per 40 mg
Novantrone®					
• Mitoxantrone, sol (2 mg/mL)	20 mg MDV	58406-0640-03	885.89	J9293	per 5 mg
•	25 mg MDV	58406-0640-05	1,107.33	J9293	per 5 mg
•	30 mg MDV	58406-0640-07	1,328.83	J9293	per 5 mg
Sandostatin®					
Octreotide Acetate, sol (50 mcg/mL)	50 mcg amp	00078-0180-03	5.21	J9999*/J3490†	
Octreotide Acetate, sol (100 mcg/mL)	100 mcg amp	00078-0181-03	9.54	J9999*/J3490†	
Octreotide Acetate, sol (500 mcg/mL)	500 mcg amp	00078-0182-03	43.62	J9999*/J3490†	
Sandostatin LAR® Depot					
Octreotide Acetate, inj	10 mg	00078-0340-84	1,368.75	J9999*/J3490†	
Octreotide Acetate, inj	20 mg	00078-0341-84	1,368.75	J9999*/J3490†	
Octreotide Acetate, inj	30 mg	00078-0342-84	2,053.12	J9999*/J3490†	
Zofran®					
Ondansetron HCl, sol (2 mg/mL)	40 mg MDV	00173-0442-00	244.43	J2405	per 1 mg
Ondansetron HCl, sol (2 mg/mL)	4 mg	00173-0442-02	24.45	J2405	per 1 mg
Ondansetron HCl, sol premixed (32 mg/50 mL D5W)	32 mg bag	00173-0461-00	206.41	J2405*	per 1 mg
Neumega®					
• Oprelvekin	5 mg	58394-004-01	248.75	J2355	per 5 mg
TAXOL®					
Paclitaxel, semi-synthetic sol (6mg/ml)	30 mg	00015-3475-30	182.63	J9265	per 30 mg
	100 mg	00015-3476-30	608.76	J9265	per 30 mg
	300 mg	00015-3479-11	1,826.25	J9265	per 30 mg
Aredia®					
• Pamidronate disodium, pwd	30 mg	00083-2601-04	231.12	J2430	per 30 mg
•	90 mg	00083-2609-01	652.22	J2430	per 30 mg
Nipent®					
Pentostatin, pwd	10 mg	62701-8800-01	1,645.00	J9268	per 10 mg
Prochlorperazine, sol (5 mg/mL)	10 mL vial	00007-3343-01	41.00	J0780	
Prochlorperazine, tablets, 10 mg	100 per box	00007-3367-20	94.50		
Zantac®					
Ranitidine, sol (50 mg/2 mL)	2 mL	00173-0362-38	3.99	J9999*/J3490†	
Respigam®					
Respiratory syncytial virus immune globulin, human	20 mL	60574-2102-01	427.82	J1565	per 50 mg
	50 mL	60574-2101-01	717.57	J1565	per 50 mg
Rituxan®					
• Rituximab	100 mg	50242-0051-21	421.35	J9310	per 100 mg
Zanosar®					
Streptozocin, pwd	1 g	00009-0844-01	106.16	J9320	per 1 g
Vumon®					
• Teniposide, 50 mg	5 mL amp	00015-3075-19	195.78	J9999*	per 50 mg
Thioplex®					
Thiotepa, pwd	15 mg	58406-0661-02	105.58	J9340	per 15 mg
Hycamtin®					
• Topotecan HCl lyoph pwd	4 mg	00007-4201-01	603.95	J9350	per 4 mg
•	4 mg, 5s	00007-4201-05	603.95	J9350	per 4 mg
Herceptin®					
Trastuzumab	440 mg	50242-0134-60	2,262.50	J9999*/J3490†	
Neutrexin®					
• Trimetrexate glucuronate, pwd	25 mg, 10s ea.	58178-0020-10	700.00	J3305	per 25 mg
•	25 mg, 50s ea.	58178-0020-50	700.00	J3305	per 25 mg
• Trimetrexate glucuronate, sol	200 mg	58178-0021-01	560.00	J3305	per 25 mg
Urokinase, sol (5,000 IU/mL)	5,000 IU	00074-6111-01	56.26	J3364	per 5,000 IU
	9,000 IU	00074-6145-02	98.13	J3364	per 5,000 IU
Vinblastine sulfate, pwd	10 mg	55390-0091-10	21.25	J9360	per 1 mg
Vinblastine sulfate, sol (1 mg/mL)	10 mg	00469-2780-30	43.23	J9360	per 1 mg
Vincristine, preservative free sol (1 mg/mL)	1 mg	00013-7456-86	37.08	J9370	per 1 mg
	1 mg	61703-0309-06	31.75	J9370	per 1 mg
	2 mg	00013-7466-86	74.13	J9375	per 2 mg
	2 mg	61703-0309-16	38.25	J9375	per 2 mg
Vincristine, preservative free sol (5 mg/mL)	50 mg	61703-0210-11	7.47	J9380	per 5 mg
	150 mg	61703-0210-31	20.30	J9380	per 5 mg
NAVELBINE®					
Vinorelbine tartrate, sol (10 mg/mL)	1 mL	00173-0656-01	69.72	J9390	per 10 mg
	5 mL	00173-0656-44	348.58	J9390	per 10 mg

• An AWP, HCPCS code or NDC that has changed or been added has been highlighted in color.

* The drug code J9999 is defined as "not otherwise classified, antineoplastic drug." The Health Care Financing Administration (HCFA) has not assigned specific codes to these drugs.

† The drug code J3490 is defined as "unclassified drug." These drugs may or may not be defined as an unclassified drug in your area. Consult your local carrier for the appropriate code.

‡ Q0136 is the code for non-ESRD (End Stage Renal Disease) use.

+ J2405 should be used for all formulations of Zofran.

BULK RATE U.S. POSTAGE PAID MMS, Inc.

ADDRESS CORRECTION REQUESTED

ONCOLOGY THERAPEUTICS NETWORK

393 OYSTER POINT BLVD, SUITE 405
SOUTH SAN FRANCISCO, CA 94080

BP 01221

ONCOLOGY THERAPEUTICS NETWORK

September/October 1999

THE NETWORK NEWS

AN UPDATE FOR COMMUNITY-BASED ONCOLOGY PROFESSIONALS

Route To:

- ❑ Physician
- ❑ Office Manager
- ❑ Oncology Nurse
- ❑ Pharmacist
- ❑ Business Office
- ❑ _____

IN THIS ISSUE

10A

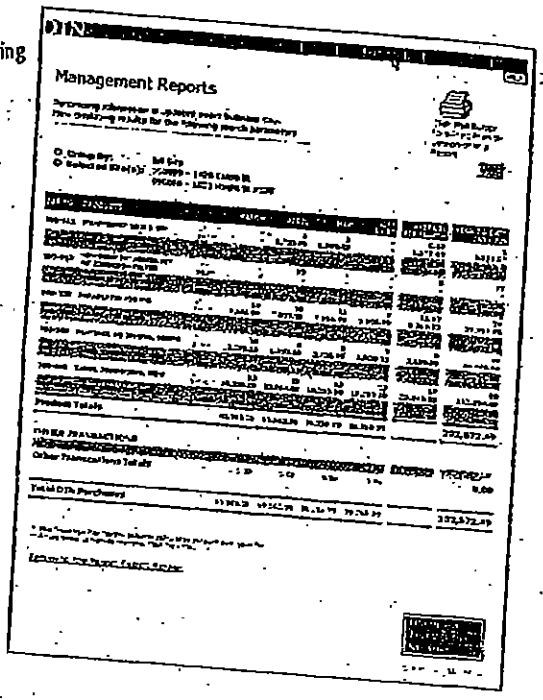
ONCOLOGY THERAPEUTICS NETWORK

Now Available!

Management Reports Online

Access Your Practice's Monthly Inventory Management Reports Online!

OTN is committed to continually improving your access to data and to addressing your concerns regarding your practice's profitably. To that end, we are happy to announce that as OTN customers, you are now able to access your monthly inventory management reports via OTN-Online.



Benefits

- ✓ Access your current monthly purchase history, which is updated daily to reflect your previous day's totals.
- ✓ Track purchase history for multiple sites.
- ✓ Compare the current month's quantity and cost, by item, to the previous three-month averages.

OTN-Online is for the exclusive use of OTN customers. You will need a password and user name assigned by OTN to access OTN-Online. Contact your OTN account representative at 1-800-482-6700 to set up an account.

otn-online.com

The articles in this newsletter are not intended to serve as rules and policies for medical practice. Primary references should be consulted. The reader is encouraged to review the manufacturer's package insert where applicable.

Comments and suggestions are welcome. Address them to: Libby Dodd, Editor, The Network News: Oncology Therapeutics Network, 395 Oyster Point Blvd., Suite 405, So. San Francisco, CA 94080.

Printed on recycled paper.

ONCOLOGY THERAPEUTICS NETWORK

Denials and Appeals

Bobbi Buell, MBA
President
Documedics

Q: *What is the difference between a denial and a claim rejection?*

A: A claim rejection occurs because the insurance carrier perceives that you have billed incorrectly. For example, you used an invalid ICD-9-CM or CPT code. The claim is then rejected because it is not "clean." When a claim is denied, generally, the claim does not support medical necessity or the appropriateness of services billed. Rejected claims for invalid coding or billing errors can be resolved by re-billing. However, denials must be appealed, and this process can take six months or more.

Q: *What does the Explanation of Benefits (EOB) say when your claim is denied?*

A: It usually says that the service delivered was not "medically necessary." However, this is somewhat misleading. Rejections for a fourth digit of nine (.9) on an ICD-9-CM diagnosis code have the same EOB message as claims rejected for "off label" use. When in doubt, call the OTN hotline or your Carrier. Hopefully, if you call the Carrier, the person will be able to correctly answer the question.

Q: *Should I appeal every claim that is denied?*

A: In most cases, we would say a resounding "Yes." Here is decision criteria you can use.

- The dollar amount of the claim: Claims for under $50.00 may not be worth the effort to appeal. However, it is important to look at future claims and their dollar amounts as much as the claim in question.
- The precedent being set: Some claims must be appealed based upon the damage that will be done to your clinic and to all other cancer providers in your area. There are carriers who routinely violate State and Federal Cancer Coverage laws for "off label" use of drugs. If providers do not take a stand, these laws will not be effective.
- Prevention of future hassles: There are certain instances where, if you do not appeal, Medicare may surmise that you have filed a "false claim." Repeated billing may lead to a fraud investigation. It is best to appeal these types of claims as soon as possible before a larger problem arises. An example of this may be a consultation claim that is reduced by Medicare, which states that a consultation was not indicated for that patient. Nobody would want to see this done repeatedly.

Q: *What's the best way to write an appeal?*

A: The very first step should be to ascertain why the claim has been reduced or not paid. I have seen appeals written for claims that could simply have been re-billed. Also, you have to make sure you are addressing the right issue. After that, we suggest that you do the following things:

1. Gather all pertinent information about the case: All supporting documentation about that PATIENT is necessary to support what you did for them. This means consultations, pathology reports, documentation of other failed therapies, etc.
2. Gather all pertinent information about the therapy: Get all articles, abstracts, or other information relative to the appropriateness of the therapy for this patient. Pharmaceutical companies are very helpful in this regard.
3. Write a concise, one-page letter summarizing the medical necessity of treatment: If you have Medicare or state law on your side, this should be in the body of the letter. Copy your lawyer, the insurance commissioner, or Congressman, if you believe that the denial was legally unjust. Stay away from editorial comments about the demise of healthcare or poor drug pricing, etc. These can be harmful to this and future claims.

Q: *What if you lose and there is a lot of money at stake?*

A: For private insurance companies, you need to check your contract to see what the next steps are. If your contract does not state this, you have just learned a hard lesson about contracts. If a great deal of money is at stake, contact an attorney and see if further action can be taken. For Medicare, the following steps can be taken after the initial appeal:

- **FAIR HEARING:** This step must be initiated within 60 days after the initial denial. The value of all claims must be over $500.00. There are three forms of fair hearings: on the record (write-in), telephonic, and in person.
- **ADMINISTRATIVE LAW JUDGE:** This step must be initiated within 60 days after a Fair Hearing is denied. The value of all claims must be over $1,000.00. ALJ hearings are always in person.

ONCOLOGY THERAPEUTICS NETWORK

Anzemet®
dolasetron mesylate

Hoechst Marion Roussel's *5-HT$_3$ Receptor Antagonist*

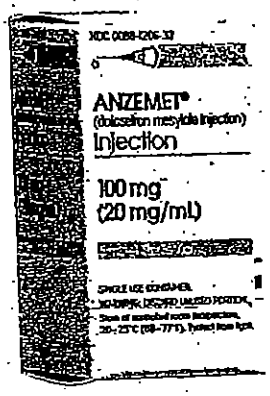
Excellent Efficacy and Safety Profile

- **Anzemet Injection** is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin.
- **Anzemet Tablets** are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses.
- **Proven Efficacy and Simplicity** — Anzemet injection can be safely infused intravenously as rapidly as 100 mg/30 seconds or diluted in compatible IV solutions and infused over 15 minutes. The recommended oral dosage of Anzemet is 100 mg given within one hour before chemotherapy.

J-CODES

Injections: J1260, per 1 mg

Tablets: Q0180, per 100 mg



For more information on dosing and administration, please contact your Hoechst Marion Roussel representative.

Great Value!

CATALOG NUMBER	NDC	BRAND NAME	ITEM	UNIT SIZE	ORDER QUANTITY	PRICE/UNIT	AWP
900-250	0088-1206-32	Anzemet	dolasetron mesylate	100 mg vial	1	$72.80	$155.88
970-300	0088-1203-05	Anzemet	dolasetron mesylate	100 mg tablets	5	$301.00	$343.20
970-305	0088-1203-29	Anzemet	dolasetron mesylate	100 mg tablets blister pack	5	$301.00	$686.40
970-310	0088-1203-43	Anzemet	dolasetron mesylate	100 mg tablets unit dose	10	$602.00	$686.40

Outstanding Support:

Reimbursement and Patient Assistance Program Hotline 1-888-895-2219

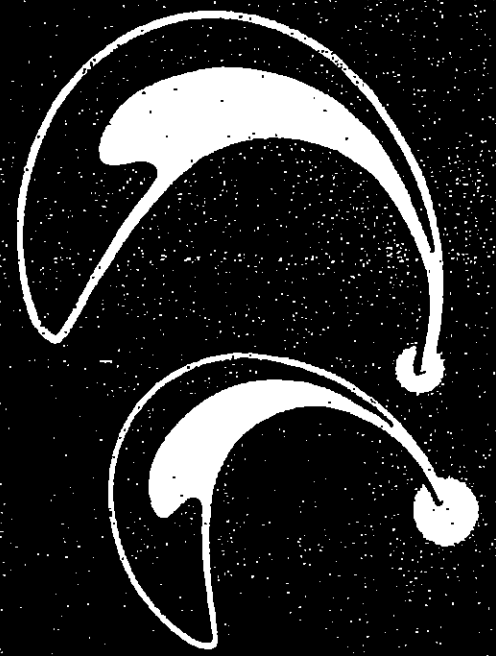
Call the Anzemet Hotline for help with reimbursement and patient assistance programs, Monday through Friday between 10 a.m. and 6 p.m. ET.

Call OTN today at 1-800-482-6700 to place your order!

Visit the website! www.anzemet.com

ONCOLOGY THERAPEUTICS NETWORK

A Program Supporting the Reimbursement of Oral Chemotherapy and Supportive Care Medicines in Physician Offices



ORCA™

An Introduction to ORCA

ORCA (Oral Reimbursement for Cancer Agents) is a free service provided by Oncology Therapeutics Network (OTN), which can simplify and expedite billing and reimbursement for oral chemotherapy and supportive care medicines in your office.*

Why participate?

- Simplifies the use of oral therapies in the physician's office
- Eliminates concerns over reimbursement delays and denials
- Service is provided "free of charge" by OTN

How does ORCA work?

There are four components to the program:

1. Enrollment in the National Supplier Clearinghouse (NSC)
2. Drug fulfillment through OTN
3. Billing, collection, and appeals of individual claims through ORCA
4. Drug replacement is guaranteed if reimbursement is not approved

Which oral medications and insurance carriers are covered by ORCA?

- Cytoxan® Tablets (cyclophosphamide tablets, USP)
- VePesid® (etoposide) Capsules

The ORCA program covers all Medicare patients. It is expected that the program will be expanded in the near future to cover additional chemotherapeutic and supportive care medicines and additional insurance carriers.

Who is eligible to participate in ORCA?

Any office-based physician practice is eligible to participate in the ORCA program.

How do I enroll in the program?

1. If you are not already an OTN customer, call 1-800-482-6700 to set up an account.
2. Once you have set up an account, or if you are already an OTN customer, call the ORCA program at 1-877-SAY-ORCA (1-877-729-6722) to request an enrollment packet.

* The ORCA program is a free service provided by OTN and is administered by AccessMED, 6900 College Boulevard, Suite 1000, Overland Park, KS 66211. AccessMED is a leading reimbursement and consulting firm focused on oncology.

ONCOLOGY THERAPEUTICS NETWORK

Rebetron™

Schering®

A combination of Rebetol (Ribavirin, USP) Capsules and Intron® A (Interferon alfa-2b, recombinant) indicated for the treatment of chronic hepatitis C in patients who have relapsed following alfa interferon therapy.

CATALOG NUMBER	NDC	BRAND NAME	ITEM	UNIT SIZE	PRICE UNIT	PRICE AWP
220-300	0085-1241-01	Rebetron	Interferon alfa-2b/Ribavirin 1200/Pak 3	3 MIU/0.5 mL	$645.00	$720.00
220-310	0085-1236-01	Rebetron	Interferon alfa-2b/Ribavirin 1200 MDV	22.8 MIU/3.8 mL; 3 MIU/0.5 mL	$645.00	$720.00
220-320	0085-1241-02	Rebetron	Interferon alfa-2b/Ribavirin 1000/Pak 3	3 MIU/0.5 mL	$584.00	$651.59
220-330	0085-1236-02	Rebetron	Interferon alfa-2b/Ribavirin 1000 MDV	22.8 MIU/3.8 mL; 3 MIU/0.5 mL	$584.00	$651.59
220-340	0085-1241-03	Rebetron	Interferon alfa-2b/Ribavirin 600/Pak 3	3 MIU/0.5 mL	$478.00	$533.64
220-350	0085-1236-03	Rebetron	Interferon alfa-2b/Ribavirin 600 MDV	22.8 MIU/3.8 mL; 3 MIU/0.5 mL	$478.00	$533.64
220-305	0085-1258-01	Rebetron	Interferon alfa-2b/Ribavirin 1200/3 MIU Pen	6 doses x 3 MIU/0.2 mL	$645.00	$720.00
220-325	0085-1258-02	Rebetron	Interferon alfa-2b/Ribavirin 1000/3 MIU Pen	6 doses x 3 MIU/0.2 mL	$584.00	$651.59
220-345	0085-1258-03	Rebetron	Interferon alfa-2b/Ribavirin 600/3 MIU Pen	6 doses x 3 MIU/0.2 mL	$478.00	$533.64

Intron® A — HSA-Free and Original Formulation

Interferon alfa-2b, recombinant*

CATALOG NUMBER	NDC	HCPCS CODE	ITEM	UNIT SIZE	QTY	PRICE UNIT	PRICE AWP
HSA-FREE SOLUTION*							
220-151	0085-1184-01	J9214	Intron A solution	3 MIU/0.5 mL	1	$31.95	$35.63
220-161	0085-1191-01	J9214	Intron A solution	5 MIU/0.5 mL	1	$53.20	$59.38
220-171	0085-1179-01	J9214	Intron A solution	10 MIU/1 mL	1	$106.40	$118.76
220-191	0085-1168-01	J9214	Intron A solution	18 MIU/MDV	1	$191.55	$213.77
220-194	0085-1133-01	J9214	Intron A solution	25 MIU/MDV	1	$266.05	$296.93
HSA-FREE SOLUTION PAKS* (Paks include six vials, six syringes, and six alcohol swabs)							
220-156	0085-1184-02	J9214	Intron A solution, Pak-3	3 MIU	6	$31.95	$35.63
220-166	0085-1191-02	J9214	Intron A solution, Pak-5	5 MIU	6	$53.20	$59.38
220-174	0085-1179-02	J9214	Intron A solution, Pak-10	10 MIU	6	$106.40	$118.76
ORIGINAL FORMULATIONS**							
220-150	0085-0647-03	J9214	Intron A powder	3 MIU/MDV	1	$31.95	$35.63
220-160	0085-0120-02	J9214	Intron A powder	5 MIU/MDV	1	$53.20	$59.38
220-170	0085-0571-02	J9214	Intron A powder	10 MIU/MDV	1	$106.40	$118.76
220-186	0085-1110-01	J9214	Intron A powder	18 MIU/MDV	1	$191.55	$213.77
220-175	0085-0285-02	J9214	Intron A powder	25 MIU/MDV	1	$266.05	$296.93
220-180	0085-0539-01	J9214	Intron A powder	50 MIU/MDV	1	$532.10	$593.81

* HSA-free formulation is recommended for intramuscular, subcutaneous, or intralesional administration. Intron A solutions for injection are not recommended for IV administration.

** Original formulation is recommended for intramuscular, subcutaneous, intralesional, or intravenous administration.

Intron® A Interferon alfa-2b, recombinant for injection Multidose Pen

CATALOG NUMBER	NDC	BRAND NAME	ITEM	UNIT SIZE	PRICE UNIT	PRICE AWP
220-158	0085-1242-01	Intron A Multidose Pen	Interferon alfa-2b, 6 doses	3 MIU Pen	$191.55	$213.77
220-168	0085-1235-01	Intron A Multidose Pen	Interferon alfa-2b, 6 doses	5 MIU Pen	$319.25	$356.29
220-178	0085-1254-01	Intron A Multidose Pen	Interferon alfa-2b, 6 doses	10 MIU Pen	$638.50	$712.58

10A

BP 01227

ONCOLOGY THERAPEUTICS NETWORK

Intron® A Dosing Guide

INDICATION	RECOMMENDED DOSAGE	RECOMMENDED VIAL SIZE
Chronic hepatitis C	3 MIU SC or IM TIW	3 MIU/0.5 mL or Pak-3 or 18 MIU MDV
Chronic hepatitis B	30 - 35 MIU/week SC or IM (5 MIU qd or 10 MIU TIW x 16 weeks)	5 MIU/0.5 mL or Pak-5 or 10 MIU/1.0 mL or Pak-10
Malignant melanoma	Induction: 20 MIU/m² IV 5 consecutive days/week x 4 weeks Maintenance: 10 MIU/m² TIW SC x 48 weeks	50 MIU powder/1.0 mL 18 MIU powder/1.0 mL
Hairy cell leukemia	2 MIU/m² SC or 1 MIU TIW	5 MIU/0.5 mL or Pak-5 or 10 MIU/1.0 mL or Pak-10 or 18 MIU MDV
AIDS-related Kaposi's sarcoma	30 MIU/m² SC or IM TIW	50 MIU/1.0 mL powder
Condylomata acuminata	1 MIU TIW (alternate days) x 3 weeks	5 MIU/0.5 mL or Pak-5 or 10 MIU/1.0 mL or Pak-10

Intron combination therapy has been approved for naive patients and relapser patients with hepatitis C.

BODY WEIGHT	REBETOL CAPSULES	INTRON A INJECTION
≤ 75 kg	2x200-mg capsules a.m. 3x200-mg capsules p.m. daily p.o.	3 MIU 3 times weekly s.c.
> 75 kg	3x200-mg capsules a.m. 3x200-mg capsules p.m. daily p.o.	3 MIU 3 times weekly s.c.

LEUKINE® Liquid (GM-CSF, sargramostim)

From Immunex Corporation immunex®

- ✓ Easier to Use
- ✓ Bioequivalent to Lyophilized Powder
- ✓ LEUKINE Liquid Quick Reference Guide Available from Immunex
- ✓ Multi-Dose Vial
- ✓ Saves Time
- ✓ Less Waste and Saves Money

CATALOG NUMBER	NDC	ITEM	UNIT SIZE	PRICE/UNIT	AWP
[illegible]	58406-0050-30	GM-CSF (sargramostim), solution	500 mcg MDV	$225.00	$269.71

Choice of Payment Terms

Only through OTN! Customers have four payment terms options:

- 1% 30, Net 60 Days
- 2% Upon Receipt of Order
- Net 75 Days
- Credit Card, Upon Receipt of Order

Reimbursement Support

Contact the Immunex Reimbursement Hotline at

1-800-321-4669

Bill for Leukine with J2820 per 50 mcg.

NCOLOGY
E UTICS
ETWORK

ONCOLOGY DRUG UPDATES

Ambulatory Payment Classifications: Potential Impact on the Oncology Community

Claire E. Gilmore
Pharm.D.
BCOP

Medicare's spending for facility-based outpatient services has grown substantially in the 1990s. To reduce Medicare Part A outpatient hospital expenditures, the Balanced Budget Act of 1997 directed the Health Care Financing Administration (HCFA), the federal agency that administers Medicare, to implement a prospective payment system (PPS) for hospital outpatient services provided through the Medicare program. In September 1998, the HCFA released its proposed Ambulatory Payment Classification (APC) regulations that group similar hospital services together and reimburse each service within a particular APC at a fixed price. Similar to the Diagnostic Related Grouping (DRG) system for inpatient services, APCs are based on averages; some services will be reimbursed at more than the cost and other services at less than the cost. Congress authorized the HCFA to use its discretion in excluding certain services; however, outpatient cancer treatment is included in the proposed APC regulations.

HCFA developed the reimbursement payment rate using single-procedure bills and Medicare claims data from 1995 and 1996 projected forward using estimated inflation costs. The APCs do not reflect any changes in cancer care since 1996, including new chemotherapy, biologic agents, and chemotherapy indications. Only hospital outpatient service payments reimbursed by the current Medicare system would be replaced by APC payments. Payments for physician services would continue to be made under the physician fee schedule. The proposed APC regulations capitate oncology services and give hospitals an incentive to use older, more moderately priced agents, thereby prohibiting patient access to newer, potentially more effective cancer treatments.

Disadvantages of Proposed APC Regulations

Chemotherapy

Medicare currently reimburses providers for chemotherapy based on the average wholesale price (AWP) less five percent. Actual chemotherapy drug costs are generally lower than the AWP; as a result of this difference, oncology practices recoup their costs and maintain a profit margin. The proposed APC system groups chemotherapy drugs into one of four categories, with these corresponding payments paid to the provider for these drugs: (1) $52.70, (2) $85.63, (3) $146.43, and (4) $211.29. New chemotherapy drugs, currently assigned an HCPC code of J9999 (nonspecified chemotherapy drug), are automatically placed in the lowest APC, resulting in gross undercompensation to the hospital. Furthermore, placement of some older drugs in higher APCs results in tremendous overcompensation. For example, a new agent such as trastuzumab (Herceptin®) or gemcitabine (Gemzar®) is assigned a maximum reimbursement of $52.70, whereas leucovorin calcium injection is assigned a reimbursement of $211.29.

Not only are these chemotherapy drug reimbursements low, but pharmacy mixing costs, supplies, and nonchemotherapy drugs are also included in the chemotherapy APC. Medicare's reimbursement plan for multiple drug treatment regimens remains uncertain. Because hospitals need to contain costs, oncologists will feel pressured to prescribe older, potentially less effective drugs.

Continued on next page

Continued from the previous page

Supportive Care Drugs

Supportive care drugs, such as antiemetics and colony-stimulating factors, do not have an APC category, but are grouped with chemotherapy drugs or nursing administration APCs. This lack of direct payment will inevitably result in more hospitalizations for supportive care measures.

Chemotherapy Infusion Services

There are three chemotherapy administration APCs and two nonchemotherapy infusion APCs for administration of intravenous fluids in conjunction with chemotherapy treatments. The highest single reimbursement is $210.28, and the units of service (i.e., duration of chemotherapy drug or intravenous fluid infusions) allowed remain uncertain.

Radiation Oncology

Six APC categories cover radiation oncology, with radioelements included.

Impact of APCs on Cancer Patients

If the proposed APC regulations are implemented, the financial impact on outpatient hospital cancer centers will be devastating. HCFA projects a 29.2% decrease in revenues from APC reimbursement for large university cancer centers, and a comparable drop will occur in community hospital outpatient departments. Additionally, rural hospital cancer programs and radiation oncology centers will most likely be economically unable to survive. Oncology clinical research, which occurs primarily in university-based cancer programs, will decline. Furthermore, HCFA plans to apply the PPS to private practices if APCs work in the outpatient hospital setting.

In addition to the potentially devastating economic effects on treatment facilities, Medicare beneficiaries will be threatened with limited access to high-quality cancer treatment. Because APCs create an incentive for hospitals to put financial considerations first, clinical decision-making will be inappropriately influenced; therefore, current advances in treatment and supportive care drugs may not be made available to cancer patients.

Initially, the PPS was to be implemented by January 1, 1999. However, because of internal year 2000 (Y2K) complications, HCFA is unable to implement the PPS until after January 1, 2000, probably within the first quarter of the year. Not surprisingly, the proposed APC regulations have met resistance by physicians, nurses, cancer patient advocates, and other health care professionals. The comment period for submitting letters to HCFA in opposition to the regulations was extended three times, the last deadline being June 30, 1999. A massive response is anticipated; however, a lack of response means that the HCFA will potentially enact the APC regulations as soon as 60 days after the close of the comment period.

Potential Legislation to Protect Outpatient Cancer Treatment

To protect Medicare beneficiaries' access to the newest and best cancer treatments, U.S. Representative Gene Green, a Democrat from Texas, introduced HR 1090, the Medicare Full Access to Cancer Treatment Act (FACT), earlier this year. This bill proposes to exclude cancer treatment from the outpatient PPS and continue reimbursement on a cost-plus basis, thereby preserving patient access to optimal cancer care. Support for this legislation from bipartisan cosponsors, the Center for Patient Advocacy, the American Society of Clinical Oncology, the Association of Community Cancer Centers, the Oncology Nursing Society, and the National Alliance of Breast Cancer Organizations has been overwhelming. The bill was referred to several House committees and subcommittees, but no floor action has occurred yet.

ONCOLOGY THERAPEUTICS NETWORK

ONCOLOGY DRUG UPDATES

Bladder Cancer: Treatment Update 1999

Claire E. Gilmore
Pharm.D.
BCOP

Transitional cell carcinoma (TCC) of the urinary bladder, which represents 90% to 95% of all bladder cancers, is the fourth most common cancer among American men. Approximately 80% of diagnosed bladder cancers are superficial – that is, they are restricted to the epithelium or have invaded the lamina propria, but not the muscle. The pathogenesis of TCC is linked to the loss of the 9q allele, a tumor suppressor gene. Additionally, p53 mutations, tobacco use, and long-term indwelling bladder catheters appear to be associated with the development of bladder cancer. Measures to prevent bladder cancer that are under investigation include use of vitamin A and retinoids (e.g., fenretinide).

Treatment Overview

Superficial, or noninvasive, bladder cancer is often curable; depth of invasion into the bladder wall and degree of tumor differentiation determine the prognosis. Generally, palliation is the goal for patients with either deeply invasive tumors or distant metastases. Biomarkers are being increasingly used in the management of bladder cancers, in detection (e.g., ImmunoCyt®, NMP22), as prognostic markers (e.g., p53, retinoblastoma [*RB*] gene), and as intermediate end points for evaluating chemopreventive strategies (e.g., modulation of G-actin expression).

Superficial (Noninvasive) Disease

The treatment of choice for superficial bladder cancer (i.e., Stage Tis, Ta, T1) is transurethral resection (TUR) performed using either electrosurgery with fulguration (i.e., destruction of the tumor by electrical sparks) or laser surgery. Intravesical therapy is sometimes used with TUR to prevent recurrence or disease progression in high-risk patients or to treat patients with multiple tumors. Intravesical therapy is administered directly to the bladder using a Foley catheter, concentrating the medication at the tumor site. Bacillus Calmette-Guérin (BCG), an immunotherapeutic agent, is the most commonly used agent for intravesical administration; chemotherapy drugs, including thiotepa, mitomycin, doxorubicin, and epirubicin, are also used (Table 1).

Approximately 30% of patients do not respond to BCG therapy. Tumors may also recur without continued treatment. In 1998, the Food and Drug Administration approved valrubicin, an anthracycline for intravesical administration, for patients with BCG-refractory carcinoma in situ. A number of immunotherapeutic agents, including interferon alfa-2b*, bropirimine, keyhole-limpet hemocyanin (KLH), and photodynamic therapy (PDT), have also been investigated for BCG-refractory patients. Bropirimine is an oral immunomodulator that induces production of endogenous interferons, interleukin-1, and tumor necrosis factor. KLH, a nonspecific immune stimulator with no toxicity, is under investigation as an intravesical agent. PDT selectively destroys

Continued on next page

Table 1. *Selected Treatment Regimens for Bladder Cancer*[1]

Regimen/Drug Name	Dose and Administration
Intravesical Therapy	
BCG	1 vial in 50 mL preservative-free normal saline weekly x 6 wk
Thiotepa	30–60 mg in 30–60 mL normal saline weekly x 4 wk
Mitomycin C	40 mg in 40 mL sterile water or normal saline repeated up to 3 times weekly to a total of 20 doses
Interferon alfa-2b	5 MU/m2 SC 3 x wk GM-CSF 5 mcg/kg SC qd
Epirubicin	30–50 mg in 50 mL normal saline q wk x 4–8 wk
Valrubicin	800 mg in 75 mL normal saline weekly x 6 wk
Combination Chemotherapy	
CMV	Methotrexate 30 mg/m² IV days 1, 8 followed by cisplatin 100 mg/m² IV 24 h later + vinblastine 4 mg/m² IV days 1, 8 q 4 wk
M-VAC	Methotrexate 30 mg/m² IV days 1, 15, 22 + cisplatin 70 mg/m² IV day 2 + vinblastine 3 mg/m² IV days 2, 15, 22 + doxorubicin 30 mg/m² IV day 2 q 4 wk
CISCA	Cyclophosphamide 650 mg/m² IV day 1 + doxorubicin 50 mg/m² IV day 1 + cisplatin 100 mg/m² IV day 2 q 3–4 wk
VIG	Vinblastine 0.11 mg/kg/d IV days 1–2 + ifosfamide 1,200 mg/m² IV days 1–5 + gallium nitrate 300 mg/m² CIV days 1–5 + calcitriol 0.5 mg/d PO days 3–5 q 3 wk
Paclitaxel + Cisplatin*[2]	P 225 mg/m²/over 3 h followed by CI 75 mg/m² q 3 wk
Gemcitabine + Cisplatin*[3]	G 1,000 mg/m² IV on days 1, 8, 15 + C 75 mg/m² day 2 q 4 wk

BCG = Bacillus Calmette-Guérin; C = cisplatin; CI = continuous intravenous infusion; G = gemcitabine; P = paclitaxel.

*Investigational use only.

Continued from the previous page

rapidly dividing bladder cancer cells through IV administration of a photosensitizer (e.g., Photofrin®) followed by intravesical activation of the bladder lining using laser therapy with visible light.

Alternate therapies under investigation for BCG-refractory patients include gene therapy and the use of recombinant BCG carrying the interleukin-2 gene to generate an immune response at the site of the tumor. Current gene therapy strategies include delivery of replacement genes (e.g., *RB* gene), and introduction of genes that either induce chemosensitivity (e.g., thymidine kinase) or activate an immunologic response. Both the poxvirus and adenovirus are used to deliver genes to the bladder epithelium through the intravesical route; however, poor delivery mechanisms remain a limitation to effective treatment.

Invasive Disease

Radical cystectomy remains the gold standard for the treatment of muscle-invasive bladder cancers (i.e., T2–T4, stage II and above), although more than 50% of these patients experience relapse and eventually die of metastatic disease. Radical cystectomy in men involves removal of the prostate and bladder; in women, it involves the removal of the uterus, anterior vagina, ovaries, urethra, and bladder. Following cystectomy, surgeons are increasingly using a continent urinary reservoir rather than an ostomy to achieve urinary diversion. To improve quality of life and survival times, bladder-sparing approaches, including conservative surgery, radiation therapy, and chemotherapy have been investigated. In Europe, radiation therapy alone is used to treat invasive disease; its use in the United States is limited to poor surgical candidates, such as older patients or patients with a concurrent medical condition. Neither neoadjuvant chemotherapy nor neoadjuvant radiation therapy has definitively prolonged survival times; therefore, neither approach is considered standard care. The most popular and effective bladder-sparing approach is combined-modality treatment with TUR followed by chemotherapy and radiation therapy. No randomized phase III trials have been performed yet comparing this combined-modality approach with radical cystectomy.

Cisplatin remains the most active single chemotherapy agent in the treatment of bladder cancer. However, combination chemotherapy regimens tend to produce better responses in patients with invasive bladder cancer than do single-agent therapy, and regimens have been built around cisplatin (see Table 1). The most widely used combination chemotherapy regimens are methotrexate, vinblastine, doxorubicin, and cisplatin (M-VAC) or CMV, a similar regimen that excludes doxorubicin. Cisplatin combinations, although effective, are toxic; therefore, investigators have been studying new single-agent or combination regimens to improve treatment options for advanced disease. Agents that demonstrate activity either alone or in combination regimens include paclitaxel, gemcitabine, carboplatin, gallium nitrate, docetaxel, trimetrexate, and ifosfamide (see Table 1).

Results of ongoing and future trials evaluating neoadjuvant chemotherapy, adjuvant chemotherapy after cystectomy, or chemotherapy in conjunction with external beam radiation therapy will help clarify the impact of these treatments on local tumor control, prevention of distant metastases, and preservation of the bladder.

References

1. Dorr VJ, Morris D, Lorber M. Chemotherapy programs. In: Perry MC, ed. *The Chemotherapy Sourcebook*. 2nd ed. Baltimore, Md: Williams and Wilkins; 1996:856-857.
2. Dreicer R, Roth B, Upsitz S, et al. E2895 cisplatin and paclitaxel in advanced carcinoma of the urothelium: a phase II trial of the Eastern Cooperative Oncology Group [abstract]. *Proc Am Soc Clin Oncol*. 1998;17:320a. Abstract 1233.
3. Kaufman D, Stadler W, Carducci M, et al. Gemcitabine plus cisplatin in metastatic transitional cell carcinoma: final results of a phase II study [abstract]. *Proc Am Soc Clin Oncol*. 1998;17:320a. Abstract 1235.
4. O'Donnell RT, Dea G, Meyers FJ. A phase II trial of concomitant interferon alfa-2b and granulocyte-macrophage colony-stimulating factor in patients with advanced renal cell carcinoma. *J Immunother Emphasis Tumor Immunol*. 1995;17:58-61.

ONCOLOGY THERAPEUTICS NETWORK

ONCOLOGY DRUG UPDATES

ODAC Recommendations and Recent FDA Approvals

The Food and Drug Administration's (FDA's) Oncologic Drugs Advisory Committee (ODAC) met in June 1999 and recommended accelerated approval of epirubicin hydrochloride injection (Ellence®, Pharmacia & Upjohn) as a component of adjuvant therapy in breast cancer patients with involved axillary nodes following resection of primary tumor. In addition to results from several supportive studies, ODAC members reviewed data from a pivotal phase III multicenter trial in which 716 patients were randomized to receive either CMF (cyclophosphamide, methotrexate, fluorouracil) or CEF (cyclophosphamide, epirubicin, fluorouracil) as adjuvant therapy of node-positive breast cancer.[1] Patients receiving CEF had both longer 5-year relapse-free survival rates and overall survival rates compared with patients receiving CMF (63% vs. 53%, P=.009; 77% vs. 70%, P=.03). Ellence®, an isomer of doxorubicin hydrochloride, is an anthracycline antitumor agent associated with less cardiotoxicity than doxorubicin. Common adverse effects include nausea and vomiting, alopecia, and myelosuppression (e.g., neutropenia); cardiotoxicity and acute leukemia have rarely been observed in clinical trials.

Doxorubicin hydrochloride liposomal injection (Doxil®, Alza Corporation) has received accelerated approval by the FDA for an expanded indication for the treatment of metastatic ovarian cancer refractory to both paclitaxel- and platinum-based chemotherapy regimens. Doxil®, a liposomal formulation of doxorubicin with a long circulation time, is currently FDA-approved for the treatment of AIDS-related Kaposi's sarcoma. The ODAC committee primarily reviewed phase II data of Doxil, which demonstrated a modest, but acceptable 14% overall response rate that will presumably lead to tumor shrinkage. Common adverse effects reported in clinical trials with Doxil include bone marrow suppression (e.g., neutropenia, anemia), nausea and vomiting, asthenia, alopecia, hand-foot syndrome (i.e., redness, swelling, pain, and peeling skin on the hands and feet), and cardiotoxicity.

The FDA also approved an expanded indication for amifostine (Ethyol®, U.S. Bioscience and Alza Corporation) for the reduction of moderate to severe xerostomia (e.g., a chronic dry mouth condition) in patients undergoing postoperative radiation therapy for head and neck cancer. Ethyol® was FDA-approved in 1996 for the reduction of cisplatin-induced renal toxicity in patients with ovarian and non-small cell lung cancer. Pivotal data supporting this indication came from a phase III multicenter trial of 315 head and neck cancer patients randomized to receive either radiation therapy alone or amifostine 200 mg/m² 30 minutes before radiation therapy.[2] The incidence of xerostomia was significantly reduced in patients receiving Ethyol® before radiation therapy (78% vs. 50%, P <.001); furthermore, 12 months after therapy, only 34% of patients treated with Ethyol® had xerostomia, compared with 57% of patients who were not pretreated with Ethyol® (P=.0012). Common adverse effects observed with Ethyol® are moderate to severe nausea and vomiting, hypotension, fever, skin reactions, dizziness, fatigue, sneezing, and flushing.

References

1. Levine MN, Bramwell VH, Pritchard KI, et al, for the National Cancer Institute of Canada Clinical Trials Group. Randomized trial of intensive cyclophosphamide, epirubicin, and fluorouracil chemotherapy compared with cyclophosphamide, methotrexate, and fluorouracil in premenopausal women with node-positive breast cancer. *J Clin Oncol*. 1998;16:2651-2658.
2. Sauer R, Wannenmacher M, Wasserman T, et al. Randomized phase III trial of radiation ± amifostine in patients with head and neck cancer [abstract]. *Proc Am Soc Clin Oncol*. 1999;18:392a. Abstract 1516.

Average Wholesale Prices and 1999 HCPCS Codes

The Average Wholesale Prices (AWPs) and HCPCS codes for drugs commonly used in cancer treatment are provided for your use as a reimbursement resource. Products are listed alfabetically by their generic name. The AWPs are obtained from the *1999 Red Book* and the *August 1999 Red Book Update*. For drugs that have multiple manufacturers, the AWP for the product most commonly stocked by OTN is listed. For ease of use, we list the AWP information in the first three columns and the billing code and units in the two right columns. Please refer to the *Sourcebook* for a complete listing of HCPCS codes.

PRODUCT	VIAL SIZE	NDC	AVG WHSLE AWP/VIAL	HCPCS BILLING CODE	UNITS
Proleukin®					
• Aldesleukin, pwd (Interleukin-2)	22 MIU	53905-0991-01	599.75	J9015	per 22 MIU
Ethyol®					
Amifostine	500 mg	17314-7253-03	368.75	J0207	per 500 mg
Fungizone®					
Amphotericin B Oral Suspension	24 mL	00087-1162-10	26.25	J9999*/J3490*	
Blenoxane®					
Bleomycin sulfate, pwd	15 units	00015-3010-20	304.60	J9040	per 15 units
	30 units	00015-3063-01	609.20	J9040	per 15 units
Xeloda®					
• Capecitabine	150 mg	00004-1100-51	244.64		
	500 mg	00004-1101-16	1,630.91		
Paraplatin®					
Carboplatin, pwd	50 mg	00015-3213-30	104.11	J9045	per 50 mg
	150 mg	00015-3214-30	312.30	J9045	per 50 mg
	450 mg	00015-3215-30	936.90	J9045	per 50 mg
BiCNU®					
Carmustine, pwd w/diluent	100 mg	00015-3012-38	103.54	J9050	per 100 mg
Platinol®-AQ					
Cisplatin, sol (1 mg/mL)	50 mg MDV	00015-3220-22	221.44	J9062	per 50 mg
	100 mg MDV	00015-3221-22	442.85	J9062	per 50 mg
Leustatin®					
• Cladribine, sol (1 mg/mL)	10 mg	59676-0201-01	541.28	J9065	per 1 mg
Cytogam®					
Cytomegalovirus immune globulin intravenous, human	50 mL	60574-3101-01	644.41	J0850	per vial
Cytoxan® lyophilized					
Cyclophosphamide, lyophilized	100 mg	00015-0539-41	6.45	J9093	per 100 mg
	200 mg	00015-0546-41	12.25	J9094	per 200 mg
	500 mg	00015-0547-41	25.71	J9095	per 500 mg
	1 g	00015-0548-41	51.43	J9096	per 1 g
	2 g	00015-0549-41	102.89	J9097	per 2 g
Cytoxan® Tablets					
Cyclophosphamide, tablets, 25 mg	100 per bottle	00015-0504-01	212.34	J8530	25 mg
Cyclophosphamide, tablets, 50 mg	100 per bottle	00015-0503-01	389.68	J8530	25 mg
Cyclophosphamide, tablets, 50 mg	1,000 per bottle	00015-0503-02	3,711.44	J8530	25 mg
Cytarabine, pwd	100 mg	55390-0131-10	6.25	J9100	per 100 mg
	500 mg	55390-0132-10	25.00	J9110	per 500 mg
	1 g	55390-0133-01	50.00	J9110	per 500 mg
	2 g	55390-0134-01	98.90	J9110	per 500 mg
DTIC-Dome®					
• Dacarbazine, pwd	200 mg	00026-8151-20	26.61	J9140	per 200 mg
DaunoXome®					
• Daunorubicin citrate liposome inj. (2 mg/mL)	50 mg	56146-0301-01	340.00	J9151	per 10 mg
Cerubidine®					
Daunorubicin HCl, pwd	20 mg	55390-0281-10	168.50	J9150	per 10 mg
DDAVP®					
• Desmopressin Acetate, sol (4 mcg/mL)	1 mL	00075-2451-01	26.67	J2597	per 4 mcg
Zinecard™					
Dexrazoxane for injection	250 mg	00013-8715-62	158.49	J1190	per 250 mg
	500 mg	00013-8725-89	316.95	J1190	per 250 mg
• Diphenhydramine HCl, sol (50 mg/1 mL)	50 mg	00641-0376-25	1.24	J1200	
Taxotere®					
Docetaxel for injection	20 mg	00075-8001-20	284.36	J9170	per 20 mg
	80 mg	00075-8001-80	1,137.43	J9170	per 20 mg
Anzemet®					
• Dolasetron mesylate, sol (20 mg/mL)	5 mL	00088-1206-32	155.88	J1260	per 1 mg
Rubex®					
Doxorubicin, pwd	50 mg	00015-3352-22	197.15	J9000	per 10 mg
	100 mg	00015-3353-22	394.29	J9000	per 10 mg
Bedford Laboratories					
Doxorubicin, pwd	10 mg	55390-0231-10	45.08	J9000	per 10 mg
	20 mg	55390-0232-10	90.16	J9000	per 10 mg
	50 mg	55390-0233-01	225.40	J9000	per 10 mg

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	AUG AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Doxorubicin, sol (2 mg/mL)	10 mg	55390-0235-10	47.35	J9000	per 10 mg
	20 mg	55390-0236-10	94.70	J9000	per 10 mg
	50 mg	55390-0237-01	236.74	J9000	per 10 mg
	200 mg MDV	55390-0238-01	945.98	J9000	per 10 mg
Adriamycin™					
Doxorubicin, RDF pwd	10 mg	00013-1086-91	53.64	J9000	per 10 mg
	50 mg	00013-1106-79	268.18	J9000	per 10 mg
	150 mg MDV	00013-1116-83	788.44	J9000	per 10 mg
Doxorubicin, pfs sol (2 mg/mL)	10 mg	00013-1136-91	56.34	J9000	per 10 mg
	20 mg	00013-1146-94	112.66	J9000	per 10 mg
	50 mg	00013-1156-79	281.68	J9000	per 10 mg
	75 mg	00013-1176-87	422.51	J9000	per 10 mg
	200 mg MDV	00013-1166-83	1,104.13	J9000	per 10 mg
DOXIL®					
Doxorubicin, HCl liposome inj. (2mg/mL)	20 mg	61471-0295-12	656.25	J9999*	
Procrit®					
Epoetin alfa	2,000 units/ mL	59676-0302-01	24.00	Q0136†	1,000 units
	3,000 units/ mL	59676-0303-01	36.00	Q0136†	1,000 units
	4,000 units/ mL	59676-0304-01	48.00	Q0136†	1,000 units
	10,000 units/ mL	59676-0310-01	120.00	Q0136†	1,000 units
	20,000 units/ 1 mL MDV	59676-0320-01	240.00	Q0136†	1,000 units
	40,000 units/ 1 mL SDV	59676-0340-01	480.00	Q0136†	1,000 units
VePesid® *Capsules*					
Etoposide, capsules, 50 mg	20 per box	00015-3091-45	884.57	J8560	50 mg
VePesid® *For Injection*					
Etoposide, injection (20 mg/mL)	100 mg MDV	00015-3095-20	136.49	J9182	per 100 mg
	150 mg MDV	00015-3084-20	204.74	J9182	per 100 mg
	500 mg MDV	00015-3061-20	665.38	J9182	per 100 mg
	1 gm MDV	00015-3062-20	1,296.64	J9182	per 100 mg
Etopophos®					
Etoposide phosphate for injection	100 mg	00015-3404-20	124.14	J9999*	per 100 mg
Fludara®					
Fludarabine phosphate, pwd	50 mg	50419-0511-06	242.25	J9185	per 50 mg
Fluorouracil, sol (50 mg/mL)	500 mg	00013-1036-91	3.20	J9190	per 500 mg
	2,500 mg	00013-1046-94	16.04	J9190	per 500 mg
	5,000 mg	00013-1056-94	32.06	J9190	per 500 mg
Neupogen®					
G-CSF (Filgrastim), sol (0.3 mg/mL)	300 mcg	55513-0530-10	165.30	J1440	per 300 mcg
	480 mcg	55513-0546-10	274.40	J1441	per 480 mcg
Gemzar®					
Gemcitabine HCl	200 mg	00002-7501-01	93.12	J9201	per 200 mg
	1 g	00002-7502-01	465.59	J9201	per 200 mg
Leukine®					
GM-CSF (Sargramostim), lyophilized	250 mcg	58406-0002-33	134.85	J2820	per 50 mcg
Leukine Liquid® (Sargramostim), solution	500 mcg	58406-0001-35	252.06	J2820	per 50 mcg
Zoladex®					
Goserelin acetate, implant	3.6 mg syringe	00310-0960-36	469.99	J9202	per 3.6 mg
	10.8 mg syringe	00310-0961-30	1,409.98	J9202	per 3.6 mg
Kytril®					
Granisetron HCl, sol (1 mg/mL)	1 mL	00029-4149-01	195.20	J1626	per 100 mcg
	4 mL	00029-4152-01	780.80	J1626	per 100 mcg
Ifex®					
Ifosfamide	1 g	00015-0556-41	141.76	J9208	per 1 g
	3 g	00015-0557-41	425.29	J9208	per 1 g
Ifex®*/Mesnex*™					
Ifosfamide (10 x 1 g)/mesna (10 x 1 g MDV)	Combo-Pack	00015-3554-27	2,356.28	J9208/J9209	
Ifosfamide (2 x 3 g)/mesna (6 x 1 g MDV)	Combo-Pack	00015-3564-15	1,413.70	J9208/J9209	
Ifosfamide (5 x 1 g)/mesna (3 x 1 g MDV)	Combo-Pack	00015-3556-26	975.14	J9208/J9209	
Venoglobulin-S					
Immune globulin intravenous, 5% sol w/IV set	2.5 g	49669-1612-01	225.00	J1561	per 500 mg
	5 g	49669-1613-01	450.00	J1561	per 500 mg
	10 g	49669-1614-01	900.00	J1561	per 500 mg
Immune globulin intravenous, 10% sol w/IV set	5 g	49669-1622-01	475.00	J1562	per 5 g
	10 g	49669-1623-01	950.00	J1562	per 5 g
	20 g	49669-1624-01	1,900.00	J1562	per 5 g
Immune globulin intravenous, 10% sol w/IV set	1 g	00026-0648-12	90.00		
	5 g	00026-0648-20	450.00		
	10 g	00026-0648-71	900.00		
	20 g	00026-0648-24	1,800.00		

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	AUG AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
• Immune globulin intravenous, 5%-10% w/IV set	2.5 g	52769-0471-72	223.75	J1561 or J1562	
	5 g	52769-0471-75	447.50	J1561 or J1562	
	10 g	52769-0471-80	895.00	J1561 or J1562	
	120 mcg	60492-0021-01	142.00	J2792	
Rho D-immune globulin intravenous	300 mcg	60492-0023-01	324.50	J2792	
	1,000 mcg	60492-0024-01	1,081.50	J2792	
Intron® A					
Interferon alfa-2b, solution HSA-free	3 MIU	00085-1184-01	35.63	J9214	per 1 MIU
	3 MIU PAK	00085-1184-02	35.63	J9214	per 1 MIU
	5 MIU	00085-1191-01	59.38	J9214	per 1 MIU
	5 MIU PAK	00085-1191-02	59.38	J9214	per 1 MIU
	10 MIU	00085-1179-01	118.76	J9214	per 1 MIU
	10 MIU PAK	00085-1179-02	118.76	J9214	per 1 MIU
	18 MIU MDV	00085-1168-01	213.77	J9214	per 1 MIU
	25 MIU MDV	00085-1133-01	296.93	J9214	per 1 MIU
Interferon alfa-2b, pwd	3 MIU MDV	00085-0647-03	35.63	J9214	per 1 MIU
	5 MIU MDV	00085-0120-02	59.38	J9214	per 1 MIU
	10 MIU MDV	00085-0571-02	118.76	J9214	per 1 MIU
	18 MIU MDV	00085-1110-01	213.77	J9214	per 1 MIU
	25 MIU MDV	00085-0285-02	296.93	J9214	per 1 MIU
	50 MIU MDV	00085-0539-01	593.81	J9214	per 1 MIU
Roferon® A					
• Interferon alfa 2a, pwd w/3 mL diluent	18 MIU	00004-1993-09	203.48	J9213	per 3 MIU
Interferon alfa 2a, sol (3 MIU/mL)	3 MIU	00004-2009-09	34.97	J9213	per 3 MIU
Interferon alfa 2a, sol (6 MIU/mL)	6 MIU	00004-2007-09	69.91	J9213	per 3 MIU
Interferon alfa 2a, sol (10 MIU/mL)	9 MIU	00004-2010-09	98.44	J9213	per 3 MIU
Interferon alfa 2a, sol (6 MIU/mL)	18 MIU	00004-2011-09	209.60	J9213	per 3 MIU
Interferon alfa 2a, sol (36 MIU/mL)	36 MIU	00004-2012-09	419.26	J9213	per 3 MIU
Camptosar®					
Irinotecan HCl injection, CPT-11 (20 mg/mL)	2 mL	00009-7529-02	231.80	J9206	per 20 mg
	5 mL	00009-7529-01	579.53	J9206	per 20 mg
Leucovorin, pwd	50 mg	55390-0051-10	18.44	J0640	per 50 mg
	100 mg	55390-0052-10	35.00	J0640	per 50 mg
	200 mg	55390-0053-01	78.00	J0640	per 50 mg
	350 mg	58406-0623-07	137.94	J0640	per 50 mg
Lupron®					
Leuprolide acetate depot, susp. (7.5 mg/mL)	7.5 mg	00300-3629-01	594.65	J9217	per 7.5 mg
	22.5 mg	00300-3346-01	1,783.95	J9217	per 7.5 mg
Lorazepam, sol (2 mg/mL)	2 mg MDV	00008-0581-04	9.85	J2060	per 2 mg
Lorazepam, sol (2 mg/mL)	20 mg MDV	00008-0581-01	87.74	J2060	per 2 mg
Lorazepam, sol (4 mg/mL)	40 mg MDV	00008-0570-01	109.66	J2060	per 2 mg
Lorazepam, sol (2 mg/mL), w/ syringe	2 mg	00008-0581-02	30.39	J2060	per 2 mg
• Mannitol, 25% sol	50 mL	00074-4031-01	1.93	J2150	per 50 mL
Mustargen®					
• Mechlorethamine HCl, pwd	10 mg	00006-7753-31	11.22	J9230	per 10 mg
Megace®					
Megestrol acetate, tablets, 20 mg	100 per bottle	00015-0595-01	75.68		
Megestrol acetate, tablets, 40 mg	100 per bottle	00015-0596-41	134.96		
	250 per bottle	00015-0596-46	330.68		
	500 per bottle	00015-0596-45	647.88		
Megace® Oral Suspension					
• Megestrol acetate, oral suspension	8 fl oz	00015-0508-42	137.24		
Alkeran®					
Melphalan hydrochloride, pwd	50 mg	00173-0130-93	364.74	J9245	per 50 mg
Melphalan hydrochloride, tablets, 2 mg	50 per bottle	00173-0045-35	104.11	J8600	2 mg
Mesnex™					
• Mesna, sol (100 mg/mL)	1 g MDV	00015-3563-02	183.01	J9209	per 200 mg
Methotrexate, pwd	20 mg	58406-0673-01	5.03	J9250	per 5 mg
	1,000 mg	58406-0671-05	61.44	J9260	per 50 mg
Methotrexate, pres. free sol (25 mg/mL)	50 mg	55390-0031-10	6.88	J9260	per 50 mg
	100 mg	55390-0032-10	8.75	J9260	per 50 mg
	200 mg	55390-0033-10	17.50	J9260	per 50 mg
	250 mg	55390-0034-10	26.88	J9260	per 50 mg
Methotrexate, sol w/pres. (25 mg/mL)	50 mg	58406-0681-14	4.75	J9260	per 50 mg
	250 mg	58406-0681-17	20.48	J9260	per 50 mg
Methotrexate, tablets, 2.5 mg	100 per bottle	00555-0572-02	362.95	J8610	2.5 mg
	36 per bottle	00555-0572-35	130.05	J8610	2.5 mg
Mutamycin®					
Mitomycin, pwd	5 mg	00015-3001-20	134.11	J9280	per 5 mg
	20 mg	00015-3002-20	452.91	J9290	per 20 mg
	40 mg	00015-3059-20	915.09	J9291	per 40 mg

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	JUNE AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Novantrone[6]					
Mitoxantrone, sol (2 mg/mL)	20 mg MDV	58406-0640-03	885.89	J9293	per 5 mg
	25 mg MDV	58406-0640-05	1,107.33	J9293	per 5 mg
	30 mg MDV	58406-0640-07	1,328.83	J9293	per 5 mg
Sandostatin[1]					
• Octreotide Acetate, sol (50 mcg/mL)	50 mcg amp	00078-0180-03	6.07	J9999*/J3490†	
• Octreotide Acetate, sol (100 mcg/mL)	100 mcg amp	00078-0181-03	11.77	J9999*/J3490†	
• Octreotide Acetate, sol (500 mcg/mL)	500 mcg amp	00078-0182-03	56.80	J9999*/J3490†	
Sandostatin LAR[1] *Depot*					
Octreotide Acetate, inj	10 mg	00078-0340-84	1,368.75	J9999*/J3490†	
Octreotide Acetate, inj	20 mg	00078-0341-84	1,368.75	J9999*/J3490†	
Octreotide Acetate, inj	30 mg	00078-0342-84	2,053.12	J9999*/J3490†	
Zofran[2]					
Ondansetron HCl, sol (2 mg/mL)	40 mg MDV	00173-0442-00	244.43	J2405	per 1 mg
Ondansetron HCl, sol (2 mg/mL)	4 mg	00173-0442-02	24.45	J2405	per 1 mg
Ondansetron HCl, sol premixed (0.1 mg/50 mL D5W)	32 mg bag	00173-0461-00	206.41	J2405+	per 1 mg
Neumega[2]					
Oprelvekin	5 mg	58394-004-01	248.75	J2355	per 5 mg
TAXOL[2]					
Paclitaxel, semi-synthetic sol (6mg/ml)	30 mg	00015-3475-30	182.63	J9265	per 30 mg
	100 mg	00015-3476-30	608.76	J9265	per 30 mg
	300 mg	00015-3479-11	1,826.25	J9265	per 30 mg
Aredia[2]					
• Pamidronate disodium, pwd	30 mg	00083-2601-04	244.75	J2430	per 30 mg
	90 mg	00083-2609-01	678.31	J2430	per 30 mg
Nipent[NU]					
Pentostatin, pwd	10 mg	62701-0800-01	1,645.00	J9268	per 10 mg
Prochlorperazine, sol (5 mg/mL)	10 mL vial	00007-3343-01	41.00	J0780	
Prochlorperazine, tablets, 10 mg	100 per box	00007-3367-20	94.50		
Zantac[3]					
Ranitidine, sol (50 mg/2 mL)	2 mL	00173-0362-38	3.99	J9999*/J3490†	
Respigam[1]					
Respiratory syncitial virus immune globulin, human	20 mL	60574-2102-01	427.82	J1565	per 50 mg
	50 mL	60574-2101-01	717.57	J1565	per 50 mg
Rituxan[IM]					
• Rituximab	100 mg	50242-0051-21	421.35	J9310	per 100 mg
Zanosar[3]					
Streptozocin, pwd	1 g	00009-0844-01	106.16	J9320	per 1 g
Vumon[2]					
Teniposide, 50 mg	5 mL amp	00015-3075-19	195.78	J9999*	per 50 mg
Thioplex[3]					
Thiotepa, pwd	15 mg	58406-0661-02	105.58	J9340	per 15 mg
Hycamtin[GS]					
Topotecan HCl lyoph pwd	4 mg	00007-4201-01	603.95	J9350	per 4 mg
	4 mg, 5s	00007-4201-05	603.95	J9350	per 4 mg
Herceptin[1]					
Trastuzumab	440 mg	50242-0134-60	2,262.50	J9999*/J3490†	
Neutrexin[1]					
Trimetrexate glucuronate, pwd	25 mg, 10s ea.	58178-0020-10	700.00	J3305	per 25 mg
	25 mg, 50s ea.	58178-0020-50	700.00	J3305	per 25 mg
Trimetrexate glucuronate, sol	200 mg	58178-0021-01	560.00	J3305	per 25 mg
• Urokinase, sol (5,000 IU/mL)	5,000 IU	00074-6111-01	59.59	J3364	per 5,000 IU
	9,000 IU	00074-6145-02	103.91	J3364	per 5,000 IU
Vinblastine sulfate, pwd	10 mg	55390-0091-10	21.25	J9360	per 1 mg
• Vinblastine sulfate, sol (1 mg/mL)	10 mg	63323-0278-10	43.23	J9360	per 1 mg
• Vincristine, preservative free sol (1 mg/mL)	1 mg	00013-7456-86	43.23	J9370	per 1 mg
	1 mg	61703-0309-06	31.75	J9370	per 1 mg
	2 mg	00013-7466-86	86.46	J9375	per 2 mg
	2 mg	61703-0309-16	38.25	J9375	per 2 mg
Vincristine, preservative free sol (5 mg/mL)	50 mg	61703-0210-11	7.47	J9380	per 5 mg
	150 mg	61703-0210-31	20.31	J9380	per 5 mg
NAVELBINE[2]					
• Vinorelbine tartrate, sol (10 mg/mL)	1 mL	00173-0656-01	72.63	J9390	per 10 mg
	5 mL	00173-0656-44	363.10	J9390	per 10 mg

• An AWP, HCPCS code or NDC that has changed or been added has been highlighted in color.

* The drug code J9999 is defined as "not otherwise classified, antineoplastic drug." The Health Care Financing Administration (HCFA) has not assigned specific codes to these drugs.

† The drug code J3490 is defined as "unclassified drug." These drugs may or may not be defined as an unclassified drug in your area. Consult your local carrier for the appropriate code.

‡ Q0136 is the code for non-ESRD (End Stage Renal Disease) use.

+ J2405 should be used for all formulations of Zofran.

BULK RATE
U.S. POSTAGE
PAID
MMS, Inc.

ADDRESS
CORRECTION
REQUESTED

ONCOLOGY THERAPEUTICS NETWORK
393 OYSTER POINT BLVD., SUITE 405
SOUTH SAN FRANCISCO, CA 94080

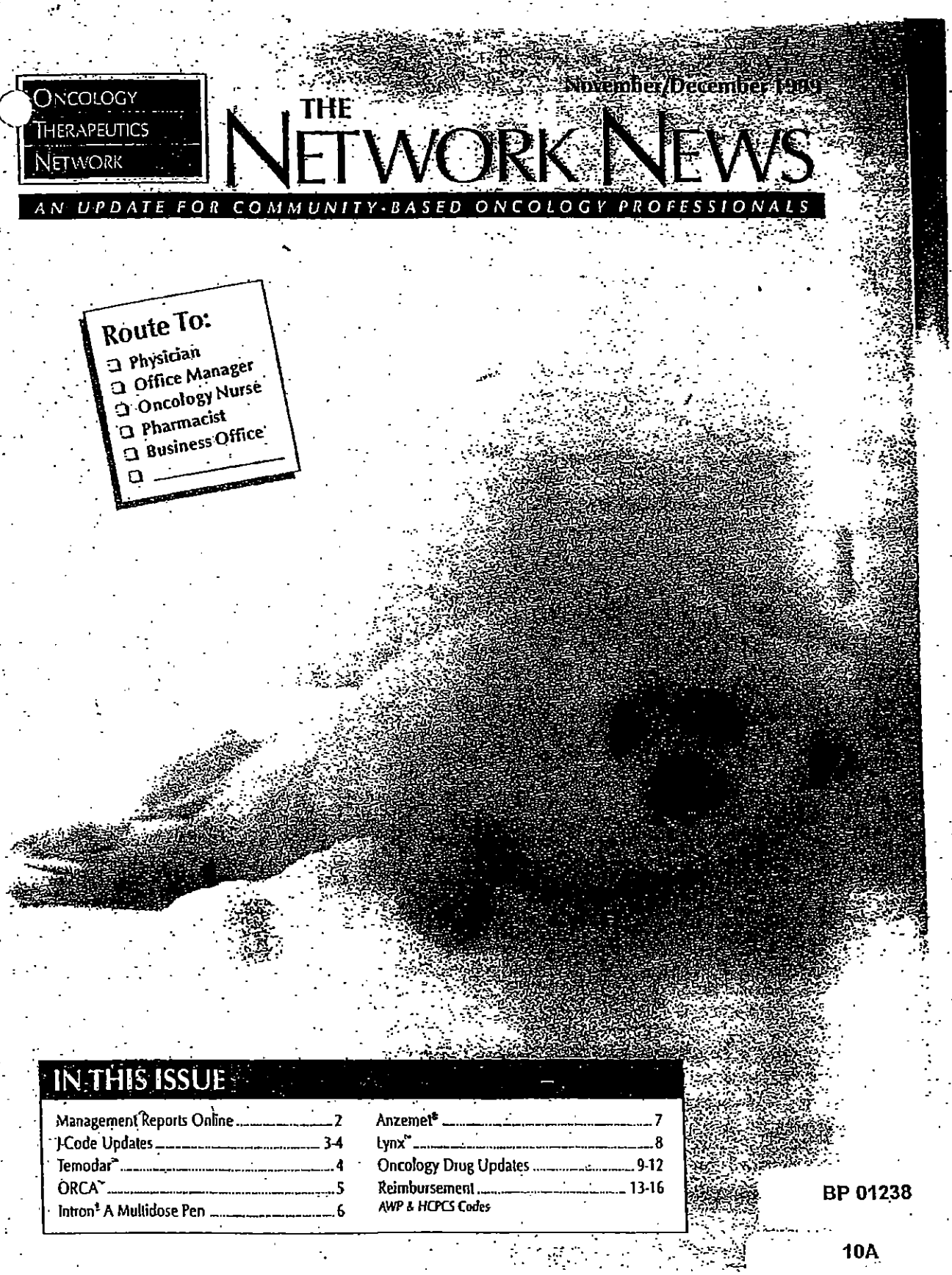
November/December 1999

ONCOLOGY THERAPEUTICS NETWORK

THE NETWORK NEWS

AN UPDATE FOR COMMUNITY-BASED ONCOLOGY PROFESSIONALS

Route To:
- ☐ Physician
- ☐ Office Manager
- ☐ Oncology Nurse
- ☐ Pharmacist
- ☐ Business Office
- ☐ _____



IN THIS ISSUE

BP 01238

10A

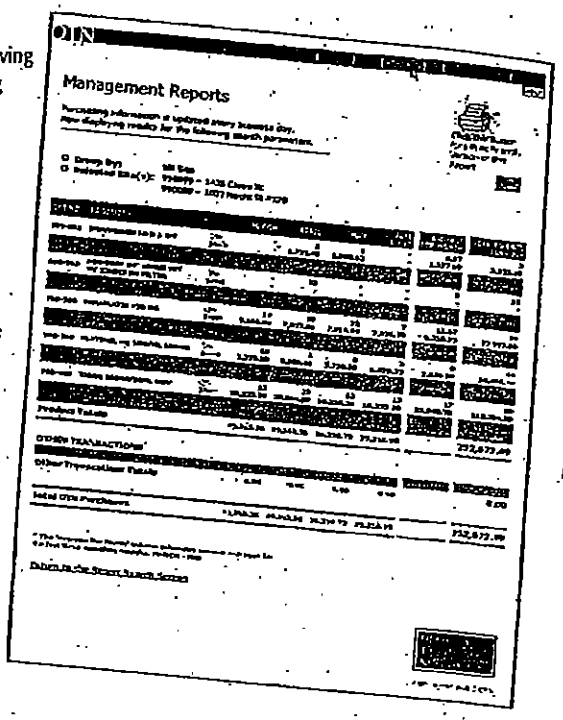
ONCOLOGY THERAPEUTICS NETWORK

Now Available!

Management Reports Online

Access Your Practice's Monthly Inventory Management Reports Online!

OTN is committed to continually improving your access to data and to addressing your concerns regarding your practice's profitably. To that end, we are happy to announce that as OTN customers, you are now able to access your monthly inventory management reports via OTN-Online.



Benefits

- ✓ Access your current monthly purchase history, which is updated daily to reflect your previous day's totals.
- ✓ Track purchase history for multiple sites.
- ✓ Compare the current month's quantity and cost, by item, to the previous three-month averages.

The Network News is distributed by Oncology Therapeutics Network Corporation.

The articles in this newsletter are not intended to serve as rules and policies for medical practice. Primary references should be consulted. The reader is encouraged to review the manufacturer's package insert where applicable.

Comments and suggestions are welcome. Address them to: Peggy Lehmann, Editor, The Network News; Oncology Therapeutics Network; 395 Oyster Point Blvd., Suite 405, So. San Francisco, CA 94080.

Printed on recycled paper.

www.otn-online.com

Reimbursement Assistance

Bobbi Buell, MBA,
President, Documedics

Oncology Therapeutics Network

Q: What CPT changes will impact oncologists?

A: There is some news for Medical Oncology and there is also news for Radiation. Check it out.

- **ALL EM Services:** When 50% of a EM service in any setting is spent counseling the patient and/or family, time is the controlling determinant of the level of service. So, if you spend 35 minutes talking to a patient about alternatives for their chemotherapy in a 40 minute visit, that would be coded to 99215. CPT adds language to clarify that counseling extends to people who have assumed responsibility for care of the patient—even if they are not family members. Medicare is not necessarily in agreement with this.
- **Consults (99241-99255):** The change in definition in consults is consistent with Medicare policy written this summer. Basically, physicians can initiate treatment the same day that a consultation is done. Also, two-way communication is necessary between you, the consulting surgeon, and the referring physician. That is, the request from a physician should be documented and a report outlining your findings/recommendations should be sent back to that physician.
- **Emergency Department Services:** 99285 has had a description change to clarify that you might not be able to get a full history and physical on the patient due to their physical condition or (lack of) mental status.
- **Critical Care Services (99291-99292):** The descriptions of 99291-99292 have been further detailed to preclude you from using these codes unless you are attending a critically ill or injured, high-risk (for big-time morbidity and mortality) patient. The good news is the patient's vital signs may be stable. Plus, these codes may be used on multiple days. Even better news is that time spent for calculation of critical care hours does not need to be bedside time. It can now be time spent coordinating patient care on the unit.
- **Starred Procedures:** Both Medicare and CPT have expanded the use of the misunderstood Modifier -25. What this means is that, if a "significant, identifiable EM service" occurs the same day as a starred procedure, you can use -25 and get paid for the EM. The trick here is that the EM has to be separately documented and medically necessary for the problem. BUT, you do NOT need to use a separate diagnosis for the EM service.
- **Aphresis:** Now there are two codes. 36520 is the old therapeutic aphresis code. 36521 is a new code describing extracorporeal affinity absorption and plasma reinfusion.
- **Venous Access Devices:** 36533, 36534, and 36535 have had a language change to substitute device for 'port.' This will allow these codes to be used for all venous access devices—ports, catheters, pumps etc. There is a new code 36550. This is for de-clotting of a port with anti-clot medication (Urokinase, Activase, Retavase). THIS IS NOT A PORT FLUSH! But, it is a small chink in the armor.
- **Radiation Oncology:** The Weekly Treatment Management codes (77419, 77420, 77425, 77430) have been deleted. Now, you have one choice for a full treatment week (3-5 fractions) and that is this new code:
  - 77427—Treatment management, five treatments, still defined as over three treatments
  - 77431—Same as present (1-2 treatments)

  Also, there was another change for Proton Beam therapy. Codes 77380-77381 have been deleted and substituted without change in description by 77520-77523.
- **Laboratory:** There are also new codes for chemistry panels. If physicians aren't confused about what they're ordering, they should be! Here are the new codes. Check out the differences from last year's descriptors:
  - 80048—Basic Metabolic Panel (same but INCLUDES calcium)
  - 80053—Comprehensive Metabolic Panel
  - 80069—Renal Function Panel
  - 80074—Acute Hepatitis Panel
  - 80076—Hepatic Function Panel
- **Sentinel Nodes:** The Radiological section has been modified to account for the bundling of radioisotope injection of sentinel node biopsies with a reference at code 78195.
- **Stem Cells:** Code 86915 has been modified to include the harvest of marrow or stem cells to wash away undesirable cells. This can be used in addition to the harvest procedure codes.
- **Immunizations:** There are now two codes for immunizations — 90471-90472, depending on the number of immunizations.
- **Chemo:** The AMA has inserted a weird note in *CPT Assistant*. It states that 96520 and 96530 are for totally implanted pumps or reservoirs. This is true of 96530—but, we use 96520 for portable pumps which are NOT implanted. We will get back to you on this one.
- **Modifiers:** The new Modifier -91 for repeat lab test the same day. This cannot be used for technical failures or bad draws. It can only be used for medically-necessary repeat lab tests.

Q: What about new ICD-9-CM codes?

A: You may ask yourself what happened to all the new ICD-9-CM codes. There are no new ICD-9-CM codes.

ONCOLOGY THERAPEUTICS NETWORK

REIMBURSEMENT ASSISTANCE

Bobbi Buell, MBA,
President, Documedics

J-Code Updates for the Year 2000

The HCFA Common Procedure Coding System (HCPCS) Editorial Panel recently announced coding changes effective for Medicare claims beginning January 1, 2000. Services provided on or after January 1, 2000, should be filed using the 2000 codes. Services rendered in 1999 should continue to be billed with the 1999 codes.

Included below are new and changed J-codes for 2000. This is not a complete list of codes and changes. Refer to the HCPCS book for a full listing. Codes may not be used until January 1, 2000. The grace period for code changes will extend to April 1, 2000.

Specific questions about these codes and requests for a complete list of code changes should be directed to your Medicare carrier.

J-CODE	BILLING UNITS	PRODUCT
J0200	100 mg	Alatrofloxacin mesylate, injection
J0290	500 mg	Ampicillin sodium, injection
J7198		Anti-inhibitor, per I.U.
J0456	500 mg	Azithromycin, injection
J8510	2 mg	Busulfan, oral
J8520	150 mg	Capecitabine, oral
J8521	500 mg	Capecitabine, oral
J0690	500 mg	Cefazolin sodium, injection
J7515	25 mg	Cyclosporine, oral
J7502	100 mg	Cyclosporine, oral
J7516	250 mg	Cyclosporine, parenteral
J1260	10 mg	Dolasetron mesylate, injection
J9001	10 mg	Doxorubicin hydrochloride, all lipid formulations (DOXIL)
J1327	5 mg	Eptifibatide, injection
J1438	25 mg	Etanercept, injection (Code may be used for Medicare when the injection is under direct supervision of the physician and not when the drug is self-administered)
J1450	200 mg	Fluconazole, injection
J7199	1 unit	Hemophilia clotting factor, not otherwise classified
J1745	10 mg	Infliximab
J1750	50 mg	Iron dextran
J7504	250 mg	Lymphocyte immune globulin, antithymocyte globulin, parenteral
J7517	250 mg	Mycophenolate mofetil, oral
J2352	1 mg	Octreotide acetate, injection
J2500	1 mg	Paricalcitol, injection
J2543	2.25 mg	Piperacillin sodium/tazobactam sodium, injection
J9270	2.5 mg	Plicamycin
J2780	2.5 mg	Ranitidine hydrochloride (ZANTAC), injection
J3240	1 mg	Thyrotropin alfa, injection
J3245	12.5 mg	Tirofiban hydrochloride, injection
J9355	10 mg	Trastuzumab (HERCEPTIN)
J9357	10 mg	Valrubicin, intravesical

A Program Supporting the Reimbursement of Oral Chemotherapy and Supportive Care Medicines in Physician Offices

ORCA™

ONCOLOGY THERAPEUTICS NETWORK

An Introduction to ORCA

ORCA (Oral Reimbursement for Cancer Agents) is a free service provided by Oncology Therapeutics Network (OTN), which can simplify and expedite billing and reimbursement for oral chemotherapy and supportive care medicines in your office.*

Why participate?

- Simplifies the use of oral therapies in the physician's office
- Eliminates concerns over reimbursement delays and denials
- Service is provided "free of charge" by OTN

How does ORCA work?

There are four components to the program:

1. Enrollment in the National Supplier Clearinghouse (NSC)
2. Drug fulfillment through OTN
3. Billing, collection, and appeals of individual claims through ORCA
4. Drug replacement is guaranteed if reimbursement is not approved

Which oral medications and insurance carriers are covered by ORCA?

- Cytoxan® Tablets (cyclophosphamide tablets, USP)
- VePesid® (etoposide) Capsules

The ORCA program covers all Medicare patients. It is expected that the program will be expanded in the near future to cover additional chemotherapeutic and supportive care medicines and additional insurance carriers.

Who is eligible to participate in ORCA?

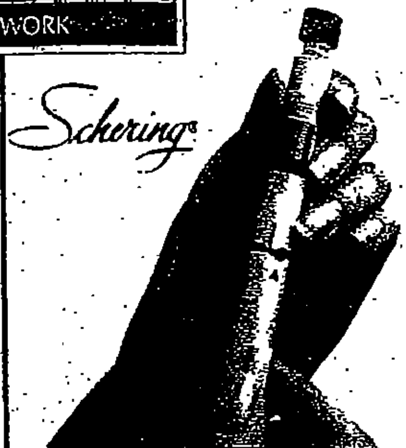
Any office-based physician practice is eligible to participate in the ORCA program.

How do I enroll in the program?

1. If you are not already an OTN customer, call 1-800-482-6700 to set up an account.
2. Once you have set up an account, or if you are already an OTN customer, call the ORCA program at 1-877-SAY-ORCA (1-877-729-6722) to request an enrollment packet.

* The ORCA program is a free service provided by OTN and is administered by AccessMED, 6900 College Boulevard, Suite 1000, Overland Park, KS 66211. AccessMED is a leading reimbursement and consulting firm focused on oncology.

ONCOLOGY THERAPEUTICS NETWORK



INTRON® A

Interferon Alfa-2b, Recombinant
for Injection

Multidose Pen

NOW AVAILABLE IN A UNIQUE DELIVERY SYSTEM

INTRON® A Multidose Pen	Total Dose and Volume	Indications
3 MIU	18 MIU (6 doses x 3 MIU/0.2 mL)*	Chronic hepatitis C
5 MIU	30 MIU (6 doses x 5 MIU/0.2 mL)*	Chronic hepatitis B, follicular lymphoma
10 MIU	60 MIU (6 doses x 10 MIU/0.2 mL)*	Chronic hepatitis B, malignant melanoma

*Each pen contains 1.5 mL; 0.3 mL extra solution is added to clear air before injection.

INTRON® A (Interferon alfa-2b, recombinant) for Injection should be stored between 2° and 8°C (36° and 46°F). INTRON® A is stable for up to 2 days at 30°C (86°F).

INTRON A therapy with the multidose pen can provide:

COMFORT
- Small needle size (30 G)
- Lower injection volume (0.2 mL)

CONVENIENCE
- Stores compactly at home and when traveling
- Disposable

ACCURACY
- Less waste
- Fewer dosing mistakes

PREFERENCE
- Preferred by >90% of patients[1-3]
- In studies with similar devices prefilled with insulin, therapeutic compliance was maintained for up to 12 months[1,2,4]

The Solution is in the Pen INTRON® A Multidose Pens

References
1. Jorgensen JOL, Flyvbjerg A, Jorgensen JT, et al. NPH insulin administration by means of a pen injector. *Diabet Med.* 1988;5:574-578.
2. Murray DP, Keenan P, Gayer E, et al. A randomized trial of the efficacy and acceptability of a pen injector. *Diabet Med.* 1988;5:750-754.
3. Fiskes AA, Gouldsbourn J. Treatment of insulin-dependent diabetes using an injection pen: control, problems and patient preferences. *Diab Res.* 1989;11:195-197.
4. Chase HP, Garg SK, Hoops SL, Harris S, Wilcox W. Use of the pen delivery system for intensive insulin therapy in college-age students with type I diabetes. *J Adolesc Health.* 1991;12:573-576.

Call OTN today at 1-800-482-6700 to place your order!

BP 01243 10A

HIGHLY CONFIDENTIAL
BMS/AWP/000095771

ONCOLOGY THERAPEUTICS NETWORK

Anzemet®
dolasetron mesylate

Hoechst Marion Roussel's *5-HT$_3$ Receptor Antagonist*

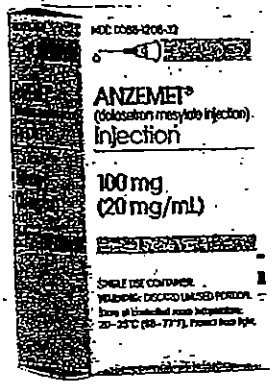
Excellent Efficacy and Safety Profile

- **Anzemet Injection** is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin.
- **Anzemet Tablets** are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses.
- **Proven Efficacy and Simplicity** — Anzemet injection can be safely infused intravenously as rapidly as 100 mg/30 seconds or diluted in compatible IV solutions and infused over 15 minutes. The recommended oral dosage of Anzemet is 100 mg given within one hour before chemotherapy.

J-CODES

Injections: J1260, per 1 mg

Tablets: Q0180, per 100 mg



For more information on dosing and administration, please contact your Hoechst Marion Roussel representative.

Great Value!

CATALOG NUMBER	NDC	BRAND NAME	ITEM	UNIT SIZE	ORDER QUANTITY	PRICE/ UNIT	AWP
900-250	0088-1206-32	Anzemet	dolasetron mesylate	100 mg vial	1	$72.80	$155.88
970-300	0088-1203-05	Anzemet	dolasetron mesylate	100 mg tablets	5	$301.00	$343.20
970-305	0088-1203-29	Anzemet	dolasetron mesylate	100 mg tablets blister pack	5	$301.00	$686.40
970-310	0088-1203-43	Anzemet	dolasetron mesylate	100 mg tablets unit dose	10	$602.00	$686.40

Outstanding Support:

Reimbursement and Patient Assistance Program Hotline 1-888-895-2219

Call the Anzemet Hotline for help with reimbursement and patient assistance programs, Monday through Friday between 10 a.m. and 6 p.m. ET.

Call OTN today at 1-800-482-6700 to place your order!

Visit the website! www.anzemet.com

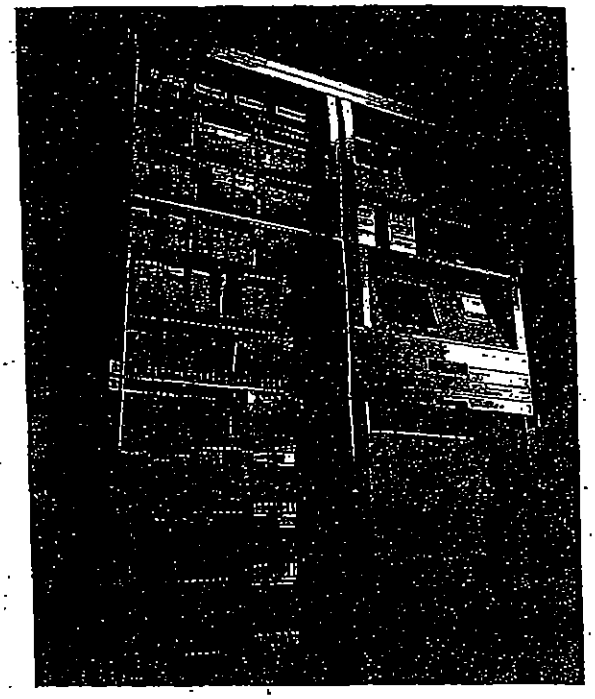
10A

BP 01244

HIGHLY CONFIDENTIAL
BMS/AWP/000095772

ONCOLOGY
THERAPEUTICS
NETWORK

Lynx™



- Controls Inventory
- Captures Lost Revenue
- Powerfully Manages Information

The Gold Standard

- ✓ Developed specifically for office-based oncology practices
- ✓ OTN has over four years experience installing and supporting Lynx
- ✓ Reference sites nationwide
- ✓ Proven scheduling and billing interfaces with common oncology practice software
- ✓ Comprehensive training program
- ✓ Ongoing technical support 24 hours a day, 7 days a week
- ✓ Nationwide field support guaranteed to respond in

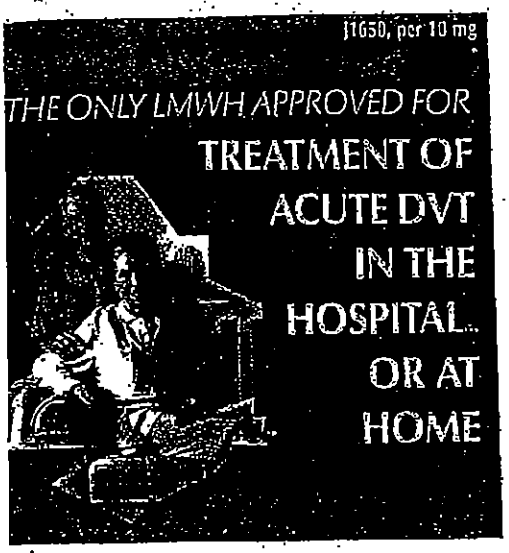
Lynx Saves Time and Money

less than four hours

- ✓ Extensive data collection and management resources
- ✓ Behind every Lynx system stands a dedicated OTN support team, including pharmacists and oncology nurses
- ✓ Automated inventory management of all products
- ✓ Reduces Inventory
- ✓ Captures lost billing charges

Over 230 oncology offices nationwide use the Lynx system

Call your OTN representative today to find out how to put the power of Lynx to work for your practice: 1-800-482-6700.



patients from the heparin drip...
: hospital or at home

iuse routine coagulation tests are relatively insensitive measures
OVENOX activity. these tests are unsuitable for monitoring in
ents with normal baseline coagulation parameters

ing e· ·comitant warfarin therapy, standard monitoring of warfarin
IN uld be performed

odic CBCs, stool occult blood tests, and platelet counts are
ommended during treatment

ivailable in 60-, 80-, and 100-mg prefilled graduated syringes

·OX cannot be used interchangeably with other low-molecular-weight he-
or unfractionated heparin. as they differ in their manufacturing process.
·r weight distribution. anti-Xa and anti-IIa activities. units. and dosage.

·idual spinal anesthesia or spinal puncture is employed. patients anti-
d or scheduled to be anticoagulated with low-molecular-weight hep-
eparinoids are at risk of developing an epidural or spinal hematoma
: result in long-term or permanent paralysis.

i these events is increased by the use of postoperative indwelling epi-
eters or by the concomitant use of drugs affecting hemostasis.

·ould be frequently monitored for signs and symptoms of neurological
·ent. See boxed WARNING.

·nts with a history of heparin-induced thrombocytopenia. LOVENOX should
d with extreme caution.

·e can occur at any site during LOVENOX therapy. An unexplained fall in
·crit or blood pressure should lead to a search for a bleeding site.

·re information, contact your local Rhône-Poulenc Rorer Representative
the RPR Medical Information and Education Center at 1-800-340-7502.

Once-a-day and q12h dosing

LOVENOX
(enoxaparin sodium) Injection

A simple solution for a serious threat

·s i summary of prescribing information on the adjacent pages

LOVENOX
(enoxaparin sodium) Injection

BRIEF SUMMARY

SPINAL / EPIDURAL HEMATOMAS

When neuraxial anesthesia (epidural/spinal anesthesia) or spinal puncture is employed, patients anticoagulated or scheduled to be anticoagulated with low molecular weight heparins or heparinoids for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis.

The risk of these events is increased by the use of indwelling epidural catheters for administration of analgesia or by the concomitant use of drugs affecting hemostasis such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk also appears to be increased by traumatic or repeated epidural or spinal puncture.

Patients should be frequently monitored for signs and symptoms of neurological impairment. If neurologic compromise is noted, urgent treatment is necessary.

The physician should consider the potential benefit versus risk before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis (see also WARNINGS, Hemorrhage, and PRECAUTIONS, Drug Interactions).

INDICATIONS AND USAGE

- Lovenox Injection is indicated for the prevention of deep vein thrombosis, which may lead to pulmonary embolism:
  - in patients undergoing hip replacement surgery, during and following hospitalization;
  - in patients undergoing knee replacement surgery;
  - in patients undergoing abdominal surgery who are at risk for thromboembolic complications. Patients at risk include patients who are over 40 years of age, obese, undergoing surgery under general anesthesia lasting longer than 30 minutes or who have additional risk factors such as malignancy or a history of deep vein thrombosis or pulmonary embolism.
- Lovenox Injection is indicated for:
  - the inpatient treatment of acute deep vein thrombosis with and without pulmonary embolism, when administered in conjunction with warfarin sodium;
  - the outpatient treatment of acute deep vein thrombosis without pulmonary embolism when administered in conjunction with warfarin sodium.
- Lovenox Injection is indicated for the prevention of ischemic complications of unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin.

See DOSAGE AND ADMINISTRATION: Adult Dosage for appropriate dosage regimens.

CONTRAINDICATIONS

Lovenox Injection is contraindicated in patients with active major bleeding, in patients with thrombocytopenia associated with a positive in vitro test for anti-platelet antibody in the presence of enoxaparin sodium, or in patients with hypersensitivity to enoxaparin sodium.

Patients with known hypersensitivity to heparin or pork products should not be treated with Lovenox Injection.

WARNINGS

Lovenox Injection is not intended for intramuscular administration.

Lovenox Injection should not be used interchangeably (unit for unit) with heparin or other low molecular weight heparins as they differ in manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units, and dosage. Each of these medications has its own instructions for use.

Lovenox Injection should be used with extreme caution in patients with a history of heparin-induced thrombocytopenia.

Hemorrhage: Lovenox Injection, like other anticoagulants, should be used with extreme caution in conditions with increased risk of hemorrhage, such as bacterial endocarditis, congenital or acquired bleeding disorders, active ulcerative and angiodysplastic gastrointestinal disease, hemorrhagic stroke, or shortly after brain, spinal, or ophthalmological surgery, or in patients treated concomitantly with platelet inhibitors.

Cases of epidural or spinal hematomas have been reported with the concomitant use of enoxaparin and epidural/spinal anesthesia or spinal puncture resulting in long-term or permanent paralysis. The risk of these events is higher with the use of post-operative indwelling epidural catheters or by the concomitant use of additional drugs affecting hemostasis such as NSAIDs (see boxed WARNING, ADVERSE REACTIONS, Ongoing Safety Surveillance, and PRECAUTIONS, Drug Interactions).

Bleeding can occur at any site during therapy with enoxaparin. An unexplained fall in hematocrit or blood pressure should lead to a search for a bleeding site.

Thrombocytopenia: Thrombocytopenia can occur with the administration of Lovenox Injection.

Moderate thrombocytopenia (platelet counts between 100,000/mm³ and 50,000/mm³) occurred at a rate of 1.3% in patients given Lovenox Injection, 1.2% in patients given heparin, and 0.8% in patients given placebo in clinical trials.

Platelet counts less than 50,000/mm³ occurred at a rate of 0.1% in patients given Lovenox Injection, in 0.2% of patients given heparin, and 0% of patients given placebo in the same trials.

Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/mm³, enoxaparin should be discontinued. Rare cases of thrombocytopenia with thrombosis have also been observed in clinical practice. The rate of incidence of this complication in actual medical practice is unknown.

PRECAUTIONS

General: Lovenox Injection should not be mixed with other injections or infusions.

Lovenox Injection should be used with care in patients with a bleeding diathesis, uncontrolled arterial hypertension or a history of recent gastrointestinal ulceration, diabetic retinopathy, and hemorrhagic stroke. Elderly patients and patients with renal insufficiency may show delayed elimination of enoxaparin. Enoxaparin should be used with care in these patients. Adjustment of enoxaparin sodium dose may be considered for low weight (<45 kg) patients and for patients with severe renal impairment (creatinine clearance <30mL/min).

If thromboembolic events occur despite enoxaparin prophylaxis, appropriate therapy should be initiated.

Laboratory Tests: Periodic complete blood counts, including platelet count, and stool occult blood tests are recommended during the course of treatment with Lovenox Injection. When administered at recommended prophylactic doses, routine coagulation tests such as Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) are relatively insensitive measures of Lovenox Injection activity and, therefore, unsuitable for monitoring. Anti-Factor Xa may be used to monitor the anticoagulant effect of Lovenox Injection in patients with significant renal impairment. If during Lovenox Injection therapy abnormal coagulation parameters or bleeding should occur, anti-Factor Xa levels may be used to monitor the anticoagulant effects of Lovenox Injection (see CLINICAL PHARMACOLOGY: Pharmacodynamics).

Drug Interactions: Unless really needed, agents which may enhance the risk of hemorrhage should be discontinued prior to initiation of Lovenox Injection therapy. These agents include medications such as: anticoagulants, platelet inhibitors including acetylsalicylic acid, salicylates, NSAIDs (including ketorolac tromethamine), dipyridamole, or sulfinpyrazone. If co-administration is intended, conduct close clinical and laboratory monitoring (see PRECAUTIONS: Laboratory Tests).

Carcinogenesis, Mutagenesis, Impairment of Fertility: No long-term studies in animals have been performed to evaluate the carcinogenic potential of enoxaparin. Enoxaparin was not mutagenic in in vitro tests including the Ames test, mouse lymphoma cell forward mutation test, and human lymphocyte chromosomal aberration test; and the in vivo rat bone marrow micronucleus test. Enoxaparin was found to have no effect on fertility or reproductive performance of male and female rats at SC doses up to 20 mg/kg/day or 141 mg/m²/day. The maximum human dose in clinical trials was 2.5 mg/kg/day or 75 mg/m²/day (for an average body weight of 70 kg, height of 170 cm, and body surface area of 1.8 m²).

Pregnancy: Teratogenic Effects: Pregnancy Category B: Teratology studies have been conducted in pregnant rats and rabbits at SC doses of enoxaparin up to 30 mg/kg/day or 211 mg/m²/day and 450 mg/kg/day, respectively. There was no evidence of teratogenic effects or fetotoxicity due to enoxaparin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Non-Teratogenic Effects: There have been a few spontaneous post-marketing reports of fetal death when pregnant women received enoxaparin. Causality of the cases has not been determined. In one case, placental hemorrhage and detachment were found in association with the fetal death. If enoxaparin is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when enoxaparin is administered to nursing women.

Pediatric Use: Safety and effectiveness of enoxaparin in pediatric patients have not been established.

ADVERSE REACTIONS

Hemorrhage: The incidence of major hemorrhagic complications during Lovenox Injection treatment has been low.

The following rates of major bleeding events have been reported during clinical trials.

Major Bleeding Episodes in Hip or Knee Replacement Surgery[a]

Indications	Lovenox 40 mg q.d. SC	Lovenox 30 mg q12h SC	Heparin 15,000 U/24h SC
	Dosing Regimen		
Hip Replacement Surgery without Extended Prophylaxis[b]		n = 786 31 (4%)	n = 541 32 (6%)
Hip Replacement Surgery with Extended Prophylaxis – Peri-operative Period[c]	n = 288 4 (2%)		
Extended Prophylaxis Period[d]	n = 221 0 (0%)		
Knee Replacement Surgery without Extended Prophylaxis[b]		n = 294 3 (1%)	n = 225 3 (1%)

[a] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease ≥2 g/dL, or transfusion of 2 or more units of blood products. Retroperitoneal and intracranial hemorrhages were always considered major. In the knee replacement surgery trials, intraocular hemorrhages were also considered major hemorrhages.

[b] Lovenox 30 mg every 12 hours SC initiated 12 to 24 hours after surgery and continued for up to 14 days after surgery.

[c] Lovenox 40 mg SC once a day initiated up to 12 hours prior to surgery and continued for up to 7 days after surgery.

[d] Lovenox 40 mg SC once a day for up to 21 days after discharge.

NOTE: At no time point were the 40 mg once a day pre-operative and the 30 mg every 12 hours post-operative hip replacement surgery prophylactic regimens compared in clinical trials.

Injection site hematomas during the extended prophylaxis period after hip replacement surgery occurred in 9% of the enoxaparin patients versus 1.8% of the placebo patients.

Major Bleeding Episodes in Abdominal and Colorectal Surgery[a]

Indications	Lovenox 40 mg q.d. SC	Heparin 5000 U q8h SC
	Dosing Regimen	
Abdominal Surgery	n = 555 23 (4%)	n = 560 16 (3%)
Colorectal Surgery	n = 673 28 (4%)	n = 674 21 (3%)

[a] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease ≥2 g/dL, or transfusion of 2 or more units of blood products. Retroperitoneal, intraocular, and intracranial hemorrhages were always considered major.

Major Bleeding Episodes in Deep Vein Thrombosis and Pulmonary Embolism Treatment[a]

Indication	Lovenox 1.5 mg/kg q.d. SC	Lovenox 1.0 mg/kg q12h SC	Heparin aPTT Adjusted i.v. Therapy
	Dosing Regimen[b]		
Deep Vein Thrombosis and Pulmonary Embolism Treatment	n = 298 5 (2%)	n = 559 9 (2%)	n = 554 9 (2%)

[a] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease ≥2 g/dL, or transfusion of 2 or more units of blood products. Retroperitoneal, intraocular, and intracranial hemorrhages were always considered major.

[b] All patients also received warfarin sodium (dose-adjusted according to PT to achieve an INR of 2.0 to 3.0) commencing within 72 hours of Lovenox or standard heparin therapy and continuing for up to 90 days.

Major Bleeding Episodes in Unstable Angina and Non-Q-Wave Myocardial Infarction

Indication	Lovenox[a] 1 mg/kg q12h SC	Heparin[a] aPTT Adjusted i.v. Therapy
	Dosing Regimen	
Unstable Angina and Non-Q-Wave MI[b,c]	n = 1578 17 (1%)	n = 1529 18 (1%)

[a] The rates represent major bleeding on study medication up to 12 hours after dose.

[b] Aspirin therapy was administered concurrently (100 to 325 mg per day).

[c] Bleeding complications were considered major: (1) if the hemorrhage caused a significant clinical event, or (2) if accompanied by a hemoglobin decrease by ≥3 g/dL or transfusion of 2 or more units of blood products. Intraocular, retroperitoneal, and intracranial hemorrhages were always considered major.

Thrombocytopenia: see WARNINGS: Thrombocytopenia.

Elevations of Serum Aminotransferases: Asymptomatic increases in aspartate (AST [SGOT]) and alanine (ALT [SGPT]) aminotransferase levels greater than three times the upper limit of normal of the laboratory reference range have been reported in up to 6.1% and 5.9% of patients, respectively, during treatment with Lovenox Injection. Similar significant increases in aminotransferase levels have also been observed in patients and healthy volunteers treated with heparin and other low molecular weight heparins. Such elevations are fully reversible and are rarely associated with increases in bilirubin.

Since aminotransferase determinations are important in the differential diagnosis of myocardial infarction, liver disease, and pulmonary emboli, elevations that might be caused by drugs like Lovenox Injection should be interpreted with caution.

Local Reactions: Mild local irritation, pain, hematoma, ecchymosis, and erythema may follow SC injection of Lovenox Injection.

Other: Other adverse effects that were thought to be possibly or probably related to treatment with Lovenox Injection, heparin, or placebo in clinical trials with patients undergoing hip or knee replacement surgery, abdominal or colorectal surgery, or treatment for DVT and that occurred at a rate of at least 2% in the enoxaparin group, are provided below.

Adverse Events Occurring at ≥2% Incidence in Lovenox Injection Treated Patients[a] Undergoing Hip or Knee Replacement Surgery

Adverse Event	Lovenox 40 mg q.d. SC Peri-operative Period n = 288[b] Severe	Lovenox 40 mg q.d. SC Peri-operative Period n = 288[b] Total	Lovenox 40 mg q.d. SC Extended Prophylaxis Period n = 131[c] Severe	Lovenox 40 mg q.d. SC Extended Prophylaxis Period n = 131[c] Total	Lovenox 30 mg q12h SC n = 1080 Severe	Lovenox 30 mg q12h SC n = 1080 Total	Heparin 15,000 U/24h SC n = 766 Severe	Heparin 15,000 U/24h SC n = 766 Total	Placebo q12h SC n = 115 Severe	Placebo q12h SC n = 115 Total
Fever	0%	8%	0%	0%	<1%	5%	<1%	4%	0%	3%
Hemorrhage	<1%	13%	0%	5%	<1%	4%	1%	4%	0%	3%
Nausea					<1%	3%	<1%	2%	0%	2%
Anemia	0%	16%	0%	<2%	<1%	2%	2%	5%	<1%	7%
Edema					<1%	2%	<1%	2%	0%	2%
Peripheral edema	0%	6%	0%	0%	<1%	3%	<1%	4%	0%	3%

[a] Excluding unrelated adverse events.

[b] Data represents Lovenox 40 mg SC once a day initiated up to 12 hours prior to surgery in 288 hip replacement surgery patients who received enoxaparin peri-operatively in an unblinded fashion in one clinical trial.

[c] Data represents Lovenox 40 mg SC once a day given in a blinded fashion as extended prophylaxis at the end of the peri-operative period in 131 of the original 288 hip replacement surgery patients for up to 21 days in one clinical trial.

Adverse Events Occurring at ≥2% Incidence in Lovenox Injection Treated Patients[a] Undergoing Abdominal or Colorectal Surgery

Adverse Event	Lovenox 40 mg q.d. SC n = 1228 Severe	Lovenox 40 mg q.d. SC n = 1228 Total	Heparin 5000 U q8h SC n = 1234 Severe	Heparin 5000 U q8h SC n = 1234 Total
Hemorrhage	<1%	7%	<1%	6%
Anemia	<1%	3%	<1%	3%
Ecchymosis	0%	3%	0%	3%

[a] Excluding unr[elated adverse events]

Adverse Events Occurring at ≥2% Incidence in Lovenox Injection Treated Patients[a] Undergoing Treatment for Deep Vein Thrombosis and Pulmonary Embolism

Adverse Event	Lovenox 1.5 mg/kg q.d. SC n = 298 Severe	Lovenox 1.5 mg/kg q.d. SC n = 298 Total	Lovenox 1.0 mg/kg q12h SC n = 559 Severe	Lovenox 1.0 mg/kg q12h SC n = 559 Total	Heparin aPTT Adjusted i.v. Therapy n = 544 Severe	Heparin aPTT Adjusted i.v. Therapy n = 544 Total
Injection Site Hemorrhage	0%	5%	0%	3%	<1%	<1%
Injection Site Pain	0%	2%	0%	2%	0%	0%
Hematuria	0%	2%	0%	<1%	<1%	2%

[a] Excluding unrelated adverse events.

Adverse Events in Lovenox Injection Treated Patients With Unstable Angina or Non-Q-Wave Myocardial Infarction: Non-hemorrhagic clinical events reported to be related to enoxaparin therapy occurred at an incidence of ≤1%.

Non-major hemorrhagic episodes, primarily injection site ecchymoses and hematomas, were more frequently reported in patients treated with SC enoxaparin than in patients treated with i.v. heparin.

Serious adverse events with Lovenox Injection or heparin in a clinical trial in patients with unstable angina or non-Q-wave myocardial infarction that occurred at a rate of at least 0.5% in the enoxaparin group, are provided below (irrespective of relationship to drug therapy).

Serious Adverse Events Occurring at ≥0.5% Incidence in Lovenox Injection Treated Patients With Unstable Angina or Non-Q-Wave Myocardial Infarction

Adverse Event	Lovenox 1 mg/kg q12h SC n = 1578 n (%)	Heparin aPTT Adjusted i.v. Therapy n = 1529 n (%)
	Dosing Regimen	
Atrial fibrillation	11 (0.70)	3 (0.20)
Heart failure	15 (0.95)	11 (0.72)
Lung edema	11 (0.70)	11 (0.72)
Pneumonia	13 (0.82)	9 (0.59)

Ongoing Safety Surveillance: Since 1993, there have been more than 80 reports of epidural or spinal hematoma formation with concurrent use of enoxaparin and spinal/epidural anesthesia or spinal puncture. The majority of patients had a post-operative indwelling epidural catheter placed for analgesia or received additional drugs affecting hemostasis such as NSAIDs. Many of the epidural or spinal hematomas caused neurologic injury, including long-term or permanent paralysis. Because these events were reported voluntarily from a population of unknown size, estimates of frequency cannot be made.

Other reports include: local reactions at the injection site (i.e., skin necrosis, nodules, inflammation, oozing), systemic allergic reactions (i.e., pruritus, urticaria, anaphylactoid reactions), vesiculobullous rash, purpura, and thrombocytosis.

OVERDOSAGE

Symptoms/Treatment: Accidental overdosage following administration of Lovenox Injection may lead to hemorrhagic complications. Injected Lovenox Injection may be largely neutralized by the slow i.v. injection of protamine sulfate (1% solution). The dose of protamine sulfate should be equal to the dose of Lovenox Injection injected: 1 mg protamine sulfate should be administered to neutralize 1 mg Lovenox Injection. A second infusion of 0.5 mg protamine sulfate per 1 mg of Lovenox Injection may be administered if the aPTT measured 2 to 4 hours after the first infusion remains prolonged. However, even with higher doses of protamine, the aPTT may remain more prolonged than under normal conditions found following administration of heparin. In all cases, the anti-Factor Xa activity is never completely neutralized (maximum about 60%). Particular care should be taken to avoid overdosage with protamine sulfate. Administration of protamine sulfate can cause severe hypotensive and anaphylactoid reactions. Because fatal reactions, often resembling anaphylaxis, have been reported with protamine sulfate, it should be given only when resuscitation techniques and treatment of anaphylactic shock are readily available. For additional information consult the labeling of Protamine Sulfate Injection, USP, products.

A single SC dose of 46.4 mg/kg enoxaparin was lethal to rats. The symptoms of acute toxicity were ataxia, decreased motility, dyspnea, cyanosis, and coma.

DOSAGE AND ADMINISTRATION

All patients should be evaluated for a bleeding disorder before prophylactic administration of Lovenox Injection. Since coagulation parameters are unsuitable for monitoring Lovenox Injection activity, routine monitoring of coagulation parameters is not required (see PRECAUTIONS, Laboratory Tests).

Adult Dosage: *Hip or Knee Replacement Surgery:* In patients undergoing hip or knee replacement surgery, the recommended dose of Lovenox Injection is 30 mg every 12 hours administered by SC injection. Provided that hemostasis has been established, the initial dose should be given 12 to 24 hours after surgery. Up to 14 days administration (average duration 7 to 10 days) of Lovenox Injection 30 mg every 12 hours has been well tolerated in controlled clinical trials. For hip replacement surgery, a dose of 40 mg once a day SC, given initially 12 (±3) hours prior to surgery, may be considered. Following the initial phase of thromboprophylaxis in hip replacement surgery patients (Lovenox Injection 30 mg every 12 hours or 40 mg once a day), continued prophylaxis with Lovenox Injection 40 mg once a day administered by SC injection for 3 weeks is recommended.

Abdominal Surgery: In patients undergoing abdominal surgery who are at risk for thromboembolic complications, the recommended dose of Lovenox Injection is 40 mg once a day administered by SC injection with the initial dose given 2 hours prior to surgery. The usual duration of administration is 7 to 10 days; up to 12 days administration has been well tolerated in clinical trials.

Treatment of Deep Vein Thrombosis and Pulmonary Embolism: In outpatient treatment, patients with acute deep vein thrombosis without pulmonary embolism who can be treated at home, the recommended dose of Lovenox Injection is 1.0 mg/kg every 12 hours administered SC. In inpatient (hospital) treatment, patients with acute deep vein thrombosis with pulmonary embolism or patients with acute deep vein thrombosis without pulmonary embolism (who are not candidates for outpatient treatment), the recommended dose of Lovenox Injection is 1.0 mg/kg every 12 hours administered SC or 1.5 mg/kg once a day administered SC at the same time every day. In both outpatient and inpatient (hospital) treatments, warfarin sodium therapy should be initiated when appropriate (usually within 72 hours of Lovenox Injection). Lovenox Injection should be continued for a minimum of 5 days and until a therapeutic oral anticoagulant effect has been achieved (International Normalization Ratio 2.0 to 3.0). The average duration of administration is 7 days; up to 17 days Lovenox Injection administration has been well tolerated in controlled clinical trials.

Unstable Angina and Non-Q-Wave Myocardial Infarction: In patients with unstable angina or non-Q-wave myocardial infarction, the recommended dose of Lovenox Injection is 1 mg/kg administered SC every 12 hours in conjunction with oral aspirin therapy (100 to 325 mg once daily). Treatment with Lovenox Injection should be prescribed for a minimum of 2 days and continued until clinical stabilization. The usual duration of treatment is 2 to 8 days. To minimize the risk of bleeding following vascular instrumentation during the treatment of unstable angina, adhere precisely to the intervals recommended between Lovenox Injection doses. The vascular access sheath for instrumentation should remain in place for 6 to 8 hours following a dose of Lovenox Injection. The next scheduled dose should be given no sooner than 6 to 8 hours after sheath removal. The site of the procedure should be observed for signs of bleeding or hematoma formation.

Administration: Enoxaparin Injection is a clear, colorless to pale yellow sterile solution, and as with other parenteral drug products, should be inspected visually for particulate matter and discoloration prior to administration.

When using Lovenox Injection ampules, to assure withdrawal of the appropriate volume of drug, the use of a tuberculin syringe or equivalent is recommended.

Lovenox Injection is administered by SC injection. It must not be administered by intramuscular injection.

Subcutaneous Injection Technique: Patients should be lying down and Lovenox Injection administered by deep SC injection. To avoid the loss of drug when using the prefilled syringes, do not expel the air bubble from the syringe before the injection. Administration should be alternated between the left and right anterolateral and left and right posterolateral abdominal wall. The whole length of the needle should be introduced into a skin fold held between the thumb and forefinger; the skin fold should be held throughout the injection. To minimize bruising, do not rub the injection site after completion of the injection. An automatic injector, Lovenox Easyinjector™, is available for patients to administer Lovenox Injection packaged in 30 mg and 40 mg prefilled syringes. Please see directions accompanying the Lovenox Easyinjector™ automatic injection device.

Keep out of the reach of children.

Rx only

Lovenox Injection prefilled and graduated prefilled syringes manufactured in France.

Lovenox Injection ampules manufactured in England.

Please see product circular for full prescribing information.

RHÔNE-POULENC

Rhône-Poulenc Rorer Pharmaceuticals Inc.
500 Arcola Road Collegeville, PA 19426

1107S

Rev

10A

BP 01247

HIGHLY CONFIDENTIAL

BMS/AWP/000095775

ONCOLOGY DRUG UPDATES

ONCOLOGY THERAPEUTICS NETWORK

gh-Dose Chemotherapy with Stem Cell Transplantation in Breast Cancer: ta from the American Society of Clinical Oncology Annual Meeting

Claire E. Gilmore, Pharm.D., BCOP

High-dose chemotherapy (HDC) with stem cell transplantation (SCT) as breast cancer treatment was the topic of the plenary session at this year's American Society of Clinical Oncology (ASCO) annual meeting in Atlanta, Georgia. Data from three studies of HDC with SCT as adjuvant therapy for high-risk primary breast cancer and one study in metastatic breast cancer (MBC) were presented at the highly anticipated session, with an audience including more than 12,000 physicians, patients, health care professionals, and patient advocacy groups. Although not presented at the plenary session, a fifth HDC-SCT study in MBC patients also received much publicity.

Results of the studies, which were released a month before the meeting in abstract form, have captured the attention of both oncologists and patients. Four of the five studies showed comparable outcomes between HDC with SCT and chemotherapy, and one study demonstrated improved outcomes with HDC with SCT. However, study investigators and plenary session discussants noted that the study results are preliminary, and oncologists must continue to educate their patients and encourage participation in clinical trials.

HDC With SCT as Adjuvant Therapy for High-Risk Primary Breast Cancer

Three, large, phase III randomized trials focused on HDC with SCT as adjuvant therapy for patients with high-risk primary breast cancer.[1-3]

CALGB/SWOG/NCIC US Study

Dr William Peters, of the Karmanos Cancer Institute in Detroit, presented the preliminary results of a U.S. phase III randomized study comparing HDC followed by bone marrow and peripheral blood SCT with intermediate-dose chemotherapy as adjuvant therapy of high-risk breast cancer patients with ten or more positive axillary lymph nodes.[1] The trial was supported by the CALGB (Cancer and Leukemia Group B), SWOG (Southwest Oncology Group), and NCIC (National Cancer Institute of Canada). Seven hundred eighty-five patients received four courses of cyclophosphamide, doxorubicin, fluorouracil (CAF) before being randomized to HDC (n=394) or intermediate-dose chemotherapy (n=391). HDC consisted of Stamp I (cyclophosphamide, cisplatin, BCNU), and intermediate-dose chemotherapy consisted of the same regimen in nonmyeloablative doses.

Based on an intent-to-treat analysis, event-free survival was comparable between HDC followed by SCT and intermediate-dose chemotherapy (68% vs 64%), as was overall survival (OS) (78% vs 80%). HDC was associated with fewer relapses than was intermediate dose chemotherapy (21.6% vs 32.2%). Dr. Peters prefaced and ended his presentation by stating that the short median follow-up of 37 months in this study is not sufficient enough to draw definitive outcome conclusions.

A 7.4% treatment-related mortality rate was observed in the HDC-with-SCT group compared with no treatment-related deaths in the intermediate-dose chemotherapy group. A trend toward higher transplant-related mortality with advanced age and at centers where fewer transplants were performed was observed, the latter suggesting that experience performing transplantations plays a major role in reducing treatment-related toxicities. A plenary session discussant, Dr. Karen Antman, of the Herbert Irving Comprehensive Cancer Center of Columbia University in New York City, pointed out that first-generation HDC regimens, such as Stamp I, are associated with a high mortality rate; however, she questioned the effectiveness of an HDC regimen associated with a lower mortality rate. Dr. Antman also noted that the control arm of nonmyeloablative doses of Stamp I used in this trial is not a standard adjuvant therapy.

SBCSG Trial

Dr. Jonas Bergh, of University Hospital in Lund, Sweden, reported the results of a study by the SBCSG (Scandinavian Breast Cancer Study Group) that randomized 525 high-risk breast cancer patients to receive treatment with nine cycles of an individually tailored fluorouracil, epirubicin, and cyclophosphamide (FEC) regimen or three cycles of standard FEC followed by Stamp V HDC (cyclophosphamide, thiotepa, carboplatin) with SCT.[2] Eligible patients were younger than 60 years of age, with eight or more positive axillary lymph nodes. At a median follow-up of 27.1 months, both relapse-free survival (RFS) and OS rates were similar between the two treatment groups. A trend toward fewer relapses was observed in the tailored FEC group compared with the HDC group (66 vs 92).

Patients in the HDC group experienced more acute toxicities, including anorexia, diarrhea, nausea, vomiting, stomatitis and infections. Interestingly, late toxicities were a problem in the tailored FEC group, with eight patients developing acute myeloid leukemia (n=5) or myelodysplastic syndrome (n=3) following treatment. In her discussion of this study, Dr. Antman pointed out that cumulative chemotherapy doses were higher in the tailored FEC group compared with the HDC group, and questioned whether more patients in the tailored FEC group will develop leukemia with longer follow-up.

South African Study

Dr. Werner Bezwoda, of the University of Witwatersrand Medical School in Johannesburg, presented results from a phase III trial that compared survival differences between standard-dose chemotherapy and HDC followed by SCT in high-risk, node-positive (greater than ten axillary lymph nodes) breast cancer patients. One hundred fifty-four patients were randomized to receive either two cycles of HDC (cyclophosphamide, mitoxantrone, etoposide) followed by SCT (n=75) or standard-dose chemotherapy with six cycles of CAF or cyclophosphamide, epirubicin, and fluorouracil (CEF) (n=79) as first-line adjuvant therapy following surgery for primary tumor.

Unlike the RFS rates reported in the other two adjuvant studies, the RFS rate in this study was statistically significantly prolonged in the HDC group compared with the standard-dose group (400 vs 190 weeks, $P < .05$). OS duration was also longer in the HDC group compared with the standard-dose chemotherapy group (400 vs 320 weeks, $P < .05$). Acute toxicities, including nausea, vomiting, and alopecia, were higher in the HDC group.

Continued on next page

Continued from the previous page

Dr. Antman commented that this study was the only trial to compare HDC with a standard adjuvant treatment regimen of CAF or CEF as the control arm, whereas the other trials used perhaps a more dose-intensive control arm. Another plenary session discussant, Dr. Gabriel Hortobagyi, of the MD Anderson Cancer Center in Houston, echoed Dr. Bezwoda's conclusions that the use of HDC as induction therapy, as studied in this trial, should be further tested.

HDC with SCT as MBC Therapy

Two studies, one presented at the plenary session and one presented at a poster session, compared conventional chemotherapy with HDC plus SCT as therapy of chemotherapy-responsive MBC.[4,5]

ECOG Study

Dr. Edward Stadtmauer, of the University of Pennsylvania Cancer Center, reported results of a large phase III study coordinated by ECOG (Eastern Cooperative Oncology Group) that compared time to progression (TTP), OS, toxicity, and quality of life differences between conventional-dose chemotherapy and HDC followed by SCT in women with chemotherapy-responsive MBC.[4] Although 553 patients were enrolled, 513 of whom were eligible for first-line induction chemotherapy with four to six cycles of CAF or cyclophosphamide, methotrexate, and fluorouracil (CMF), only 199 patients with a complete or partial response to induction chemotherapy were randomized to receive treatment with either Stamp V HDC followed by SCT (n=110) or maintenance CMF (n=89).

At a median follow-up of 37 months, OS durations were similar between the HDC and conventional chemotherapy treatment groups (24 vs 26 months). Moreover, the median TTP was equivalent between treatment groups (HDC, 9.6 months; CMF, 9 months). Patients in the HDC group experienced more acute toxicities, including infections, nausea, and diarrhea; one treatment-related death also occurred in this group.

Dr. Stadtmauer summed up his presentation with the following comments: (1) The results will not change with longer follow-up; (2) because no substantial differences in lethal toxicities occurred, survival cannot be attributed to toxicity; and (3) these data cannot be extrapolated to high-risk patients with early breast cancer. Plenary session discussant, Dr. Robert Livingston, of the University of Washington Medical Center in Seattle, asserted that because less than half of enrolled patients responded to induction chemotherapy, the study was not statistically powered to detect differences between patients who had experienced a complete response.

PEGASE 04: A French Study

Dr. Jean-Pierre Lotz, of the Hôpital Tenon in Paris, reported the results of a small, randomized study that evaluated survival differences between HDC followed by SCT and conventional anthracycline-based chemotherapy as second-line treatment of MBC.[5] Following four to six courses of conventional chemotherapy, 61 patients were randomized to receive either two to four more courses of conventional chemotherapy or HDC (mitoxantrone, cyclophosphamide, melphalan) followed by SCT.

Two-year OS rates favored the HDC group over the conventional chemotherapy group; five-year OS rates were also prolonged with HDC compared with conventional chemotherapy, although this difference was not statistically significant (29.8% vs 18.5%, $P = 0.12$). At two years, the relapse rate (RR) was higher in the conventional chemotherapy group compared with the HDC group (62.3% vs 37.5%), but at five years, RRs were similar between treatment groups (conventional chemotherapy, 90.8%; HDC, 90.7%). Because RRs were initially prolonged in the HDC group, the investigators concluded that HDC might delay relapse time in women with chemosensitive MBC, thus offering a "better quality of life with a longer off-therapy period."

Conclusions

Until recently, the majority of clinical trials evaluating HDC with SCT as breast cancer treatment, especially as adjuvant therapy, have been small, phase II studies. The data from these phase III randomized trials provide additional information to help oncologists determine the best treatment for their breast cancer patients; however, more mature data are needed to draw definitive conclusions. The results of these studies are difficult to analyze because of the following differences in the studies: HDC regimens; conventional-dose chemotherapy regimens, particularly in the adjuvant studies; patient numbers; and length of follow-up. These factors, coupled with the lack of data from randomized studies, are the impetus for investigators to initiate and complete more large, randomized trials. Throughout the plenary session discussants' presentations, the consensus was that HDC should only be used in the context of a clinical trial, and that oncologists must continue to encourage participation in clinical trials and obtain a thorough informed consent from patients being treated with HDC followed by SCT off study.

Although the controversy regarding the effectiveness of HDC with autologous SCT as breast cancer treatment has not been resolved, the results of the studies presented at the ASCO meeting are provocative. The benefits of new HDC treatment strategies, including the use of HDC with SCT for patients with chemotherapy-sensitive MBC in a complete response, single versus multiple HDC cycles, and HDC as first-line induction therapy versus HDC after induction with conventional-dose chemotherapy will undoubtedly be studied in future randomized clinical trials.

References

1. Peters W, Rosner G, Vredenburgh J, et al, for CALGB, SWOG and NCIC. A prospective, randomized comparison of two doses of combination alkylating agents (AA) as consolidation after CAF in high-risk primary breast cancer involving ten or more axillary lymph nodes (LN): preliminary results of CALGB9082/SWOG 9114/NCIC MA-13. *Proc Am Soc Clin Oncol.* 1999;18:1a. Abstract 2.
2. The Scandinavian Breast Cancer Study Group 9401. Results from a randomized adjuvant breast cancer study with high dose chemotherapy with CTC, supported by autologous bone marrow stem cells versus dose escalated and tailored FEC therapy. *Proc Am Soc Clin Oncol.* 1999;18:2a. Abstract 3.
3. Bezwoda WR. Randomized, controlled trial of high dose chemotherapy (HD-CNVp) versus standard dose (CAF) chemotherapy for high risk, surgically treated, primary breast cancer. *Proc Am Soc Clin Oncol.* 1999;18:2a. Abstract 4.
4. Stadtmauer EA, O'Neill A, Goldstein LJ, et al. Phase III randomized trial of high-dose chemotherapy (HDC) and stem cell support (SCT) shows no difference in overall survival or severe toxicity compared to maintenance chemotherapy with cyclophosphamide, methotrexate and 5-fluorouracil (CMF) for women with metastatic breast cancer who are responding to conventional induction chemotherapy: The "Philadelphia" Intergroup Study (PBT-1). *Proc Am Soc Clin Oncol.* 1999;18:1a. Abstract 1.
5. Lotz JP, Cure H, Japvier M, et al, and the PEGASE Group. High-dose chemotherapy (HD-CT) with hematopoietic stem cells transplantation (HSCT) for metastatic breast cancer (MBC): results of the French Protocol PEGASE 04. *Proc Am Soc Clin Oncol.* 1999;18:43a. Abstract 161.

ONCOLOGY DRUG UPDATES

ONCOLOGY THERAPEUTICS NETWORK

Editor's Note: This article first appeared in the September/October version of Network News. It's reprinted here with a corrected version of Table 1. This information takes precedence over previous versions.

Bladder Cancer: Treatment Update 1999

by Claire E. Gilmore, Pharm.D., BCOP

Transitional cell carcinoma (TCC) of the urinary bladder, which represents 90% to 95% of all bladder cancers, is the fourth most common cancer among American men. Approximately 80% of diagnosed bladder cancers are superficial – that is, they are restricted to the epithelium or have invaded the lamina propria, but not the muscle. The pathogenesis of TCC is linked to the loss of the 9q allele, a tumor suppressor gene. Additionally, p53 mutations, tobacco use, and long-term indwelling bladder catheters appear to be associated with the development of bladder cancer. Measures to prevent bladder cancer that are under investigation include use of vitamin A and retinoids (e.g., fenretinide).

Treatment Overview

Superficial, or noninvasive, bladder cancer is often curable; depth of invasion into the bladder wall and degree of tumor differentiation determine the prognosis. Generally, palliation is the goal for patients with either deeply invasive tumors or distant metastases. Biomarkers are being increasingly used in the management of bladder cancers, in detection (e.g., ImmunoCyt®, NMP22), as prognostic markers (e.g., p53, retinoblastoma [*RB*] gene), and as intermediate end points for evaluating chemopreventive strategies (e.g., modulation of G-actin expression).

Superficial (Noninvasive) Disease

The treatment of choice for superficial bladder cancer (i.e., Stage Tis, Ta, T1) is transurethral resection (TUR) performed using either electro-surgery with fulguration (i.e., destruction of the tumor by electrical sparks) or laser surgery. Intravesical therapy is sometimes used with TUR to prevent recurrence or disease progression in high-risk patients or to treat patients with multiple tumors. Intravesical therapy is administered directly to the bladder using a Foley catheter, concentrating the medication at the tumor site. Bacillus Calmette-Guérin (BCG), an immunotherapeutic agent, is the most commonly used agent for intravesical administration; chemotherapy drugs, including thiotepa, mitomycin, doxorubicin, and epirubicin, are also used (Table 1).

Table 1. *Selected Treatment Regimens for Bladder Cancer*[1]

Regimen/Drug Name	Dose and Administration
Intravesical Therapy	
BCG	1 vial in 50 mL preservative-free normal saline weekly x 6 wk
Interferon alfa-2b	50-100 MIU in 30 mL sterile water weekly x 12 weeks
Thiotepa	30–60 mg in 30–60 mL normal saline weekly x 4 wk
Mitomycin C	40 mg in 40 mL sterile water or normal saline repeated up to 3 times weekly to a total of 20 doses
Epirubicin	30–50 mg in 50 mL normal saline q wk x 4–8 wk
Valrubicin	800 mg in 75 mL normal saline weekly x 6 wk
Combination Chemotherapy	
CMV	Methotrexate 30 mg/m² IV days 1, 8 followed by cisplatin 100 mg/m² IV 12 h later + vinblastine 4 mg/m² IV days 1, 8 q 4 wk
M-VAC	Methotrexate 30 mg/m² IV days 1, 15, 22 + cisplatin 70 mg/m² IV day 2 + vinblastine 3 mg/m² IV days 2, 15, 22 + doxorubicin 30 mg/m² IV day 2 q 4 wk
CISCA	Cyclophosphamide 650 mg/m² IV day 1 + doxorubicin 50 mg/m² IV day 1 + cisplatin 100 mg/m² IV day 2 q 3–4 wk
VIG	Vinblastine 0.11 mg/kg/d IV days 1–2 + ifosfamide 1,200 mg/m² IV days 1–5 + gallium nitrate 300 mg/m² CIV days 1–5 + calcitriol 0.5 mg/d PO days 3–5 q 3 wk
Paclitaxel + Cisplatin[2]	P 225 mg/m²/over 3 h followed by CI 75 mg/m² q 3 wk
Gemcitabine + Cisplatin[2]	G 1,000 mg/m² IV on days 1, 8, 15 + C 75 mg/m² day 2 q 4 wk

BCG = Bacillus Calmette-Guérin; C = cisplatin; CI = continuous intravenous infusion; G = gemcitabine; P = paclitaxel.

[1]Investigational use only.

Approximately 30% of patients do not respond to BCG therapy. Tumors may also recur without continued treatment. In 1998, the Food and Drug Administration approved valrubicin, an anthracycline for intravesical administration, for patients with BCG-refractory carcinoma in situ. A number of immunotherapeutic agents, including interferon alfa-2b, bropirimine, keyhole-limpet hemocyanin (KLH), and photodynamic therapy (PDT), have also been investigated for BCG-refractory patients. Bropirimine is an oral immunomodulator that induces production of endogenous interferons, interleukin-1, and tumor necrosis factor. KLH, a nonspecific immune stimulator with no toxicity, is under investigation as an intravesical agent. PDT selectively destroys rapidly dividing bladder cancer cells through IV administration of a photosensitizer (e.g., Photofrin®) followed by intravesical activation of the bladder lining using laser therapy with visible light.

Alternate therapies under investigation for BCG-refractory patients include gene therapy and the use of recombinant BCG carrying the interleukin-2 gene to generate an immune response at the site of the tumor. Current gene therapy strategies include delivery of replacement genes (e.g., *RB* gene), and introduction of genes that either induce chemosensitivity (e.g., thymidine kinase) or activate an immunologic response. Both the poxvirus and adenovirus are used to deliver genes to the bladder epithelium through the intravesical route; however, poor delivery mechanisms remain a limitation to effective treatment.

Invasive Disease

Radical cystectomy remains the gold standard for the treatment of muscle-invasive bladder cancers (i.e., T2–T4, stage II and above), although more than 50% of these patients experience relapse and eventually die of metastatic disease. Radical cystectomy in men involves removal of the prostate and bladder; in women, it involves the removal of the uterus, anterior vagina, ovaries, urethra, and bladder. Following cystectomy, surgeons are increasingly using a continent urinary reservoir rather than an ostomy to achieve urinary diversion. To improve quality of life and survival times, bladder-sparing approaches, including conservative surgery,

Continued on next page

Continued from the previous page

radiation therapy, and chemotherapy have been investigated. In Europe, radiation therapy alone is used to treat invasive disease; its use in the United States is limited to poor surgical candidates, such as older patients or patients with a concurrent medical condition. Neither neoadjuvant chemotherapy nor neoadjuvant radiation therapy has definitively prolonged survival times; therefore, neither approach is considered standard care. The most popular and effective bladder-sparing approach is combined-modality treatment with TUR followed by chemotherapy and radiation therapy. No randomized phase III trials have been performed yet comparing this combined-modality approach with radical cystectomy.

Cisplatin remains the most active single chemotherapy agent in the treatment of bladder cancer. However, combination chemotherapy regimens tend to produce better responses in patients with invasive bladder cancer than do single-agent therapy, and regimens have been built around cisplatin (see Table 1). The most widely used combination chemotherapy regimens are methotrexate, vinblastine, doxorubicin, and cisplatin (M-VAC) or CMV, a similar regimen that excludes doxorubicin. Cisplatin combinations, although effective, are toxic; therefore, investigators have been studying new single-agent or combination regimens to improve treatment options for advanced disease. Agents that demonstrate activity either alone or in combination regimens include paclitaxel, gemcitabine, carboplatin, gallium nitrate, docetaxel, trimetrexate, and ifosfamide (see Table 1).

Results of ongoing and future trials evaluating neoadjuvant chemotherapy, adjuvant chemotherapy after cystectomy, or chemotherapy in conjunction with external beam radiation therapy will help clarify the impact of these treatments on local tumor control, prevention of distant metastases, and preservation of the bladder.

References

1. Dorr VJ, Morris D, Lorber M. Chemotherapy programs. In: Perry MC, ed. The Chemotherapy Sourcebook. 2nd ed. Baltimore, Md: Williams and Wilkins; 1996:856-857.
2. Dreicer R, Roth B, Upsitz S, et al. E2895 cisplatin and paclitaxel in advanced carcinoma of the urothelium: a phase II trial of the Eastern Cooperative Oncology Group [abstract]. *Proc Am Soc Clin Oncol.* 1998;17:320a. Abstract 1233.
3. Kaufman D, Stadler W, Carducci M, et al. Gemcitabine plus cisplatin in metastatic transitional cell carcinoma: final results of a phase II study [abstract]. *Proc Am Soc Clin Oncol.* 1998;17:320a. Abstract 1235.

ODAC Recommendations and Recent FDA Approvals

The Food and Drug Administration's (FDA's) Oncologic Drugs Advisory Committee (ODAC) met in September 1999 to review data for four drugs, one of which was UFT (uracil/tegafur, Bristol-Myers Squibb) in combination with leucovorin for the treatment of metastatic colorectal cancer. The committee unanimously voted for accelerated approval pending FDA review of recent data, including a determination that the uracil component of UFT contributes to its efficacy. UFT is a combination of tegafur, an oral 5-fluorouracil (5-FU) prodrug, and uracil, which competitively inhibits the degradation of 5-FU, resulting in a selectively higher 5-FU concentration in tumor cells. One UFT regimen studied in clinical trials was 300 mg/m²/day orally in 3 divided doses combined with leucovorin for 28 consecutive days, followed by a 7-day rest. Side effects of UFT include a dose-limiting diarrhea, hyperbilirubinemia, nausea and vomiting, and less common, mucositis and myelosuppression.

Paclitaxel (Taxol®, Bristol-Myers Squibb) has received approval for an expanded indication as a sequential therapy following doxorubicin-containing chemotherapy for the adjuvant treatment of node-positive breast cancer. Data supporting this indication came from a large study of more than 3,000 women with node-positive primary breast cancer who were randomly assigned to receive 1 of 3 doxorubicin doses combined with cyclophosphamide every 3 weeks for 4 cycles, with or without subsequent Taxol 175 mg/m² every 3 weeks for 4 cycles.[1] In this study, the use of Taxol® reduced the recurrence rate by 22% and the mortality rate by 26%. Taxol®'s current FDA-approved indications include first-line and subsequent therapy of advanced ovarian cancer, treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy, combination therapy with cisplatin for first-line treatment of patients with non-small cell lung cancer who are not surgery or radiation therapy candidates, and second-line treatment of AIDS-related Kaposi's sarcoma. Primary side effects of paclitaxel include myelosuppression, alopecia, peripheral neuropathy, and myalgia.

Two drugs reviewed by the ODAC in September did not receive approval: liposomal doxorubicin (Evacet®, The Liposome Company) in combination with cyclophosphamide for the first-line treatment of metastatic breast cancer and interferon alfa-2 (Roferon-A®, Hoffmann-La Roche) for the adjuvant treatment of node-negative stage II melanoma.

The FDA has recently approved three new agents for use in the treatment of breast cancer. In late October, paclitaxel (Taxol®, Bristol-Myers Squibb) was approved for adjuvant treatment of node-positive breast cancer administered sequentially to standard doxorubicin-containing combination chemotherapy. A survival benefit has been demonstrated only in patients with estrogen and progesterone receptor-negative tumors.

Exemestane (Aromasin®, Pharmacia & Upjohn), an aromatase inactivator, has been approved for the treatment of advanced breast cancer in postmenopausal women whose disease has progressed following tamoxifen therapy. Common toxicities associated with exemestane include hot flashes, nausea, fatigue, increased sweating, and increased appetite.

In September, the FDA approved epirubicin hydrochloride (Ellence®, Pharmacia & Upjohn) for use as a component of adjuvant therapy in patients with evidence of axillary node tumor involvement following resection of primary breast cancer.

References

1. Henderson IC, Berry D, Demetri G, et al, for CALGB, ECOG, SWOG, and NCCTG. Improved disease-free (DFS) and overall survival (OS) from the addition of sequential paclitaxel (T) but not from the escalation of doxorubicin (A) dose level in the adjuvant chemotherapy of patients (PTS) with node-positive primary breast cancer (BC). *Proc Am Soc Clin Oncol.* 1998;17:301a. Abstract 390A.

Average Wholesale Prices and 1999 HCPCS Codes

The Average Wholesale Prices (AWPs) and HCPCS codes for drugs commonly used in cancer treatment are provided for your use as a reimbursement resource. Products are listed alfabetically by their generic name. The AWPs are obtained from the *1999 Red Book* and the *November 1999 Red Book Update*.

For drugs that have multiple manufacturers, the AWP for the product most commonly stocked by OTN is listed. For ease of use, we list the AWP information in the first three columns and the billing code and units in the two right columns. Please refer to the Sourcebook for a complete listing of HCPCS codes.

PRODUCT	VIAL SIZE	NDC	AVG WHOLESALE PRICE	BILLING CODE	BILLING UNITS
Proleukin®					
Aldesleukin, pwd (Interleukin-2)	22 MIU	53905-0991-01	599.75	J9015	per 22 MIU
Ethyol®					
Amifostine	500 mg	17314-7253-03	368.75	J0207	per 500 mg
Fungizone®					
Amphotericin B Oral Suspension	25 mL	00087-1162-10	26.25	J0285	
Blenoxane®					
Bleomycin sulfate, pwd	15 units	00015-3010-20	304.60	J9040	per 15 units
	30 units	00015-3063-01	609.20	J9040	per 15 units
Xeloda®					
Capecitabine	150 mg	00004-1100-51	244.64	J8520	
	500 mg	00004-1101-16	1,630.91	J8521	
Paraplatin®					
Carboplatin, pwd	50 mg	00015-3213-30	104.11	J9045	per 50 mg
	150 mg	00015-3214-30	312.30	J9045	per 50 mg
	450 mg	00015-3215-30	936.90	J9045	per 50 mg
BiCNU®					
Carmustine, pwd w/diluent	100 mg	00015-3012-38	108.71	J9050	per 100 mg
Platinol®-AQ					
Cisplatin, sol (1 mg/mL)	50 mL MDV	00015-3220-22	221.44	J9062	per 50 mg
	100 mL MDV	00015-3221-22	442.85	J9062	per 50 mg
Leustatin®					
Cladribine, sol (1 mg/mL)	10 mL	59676-0201-01	562.80	J9065	per 1 mg
Cytogam®					
Cytomegalovirus immune globulin intravenous, human	50 mL	60574-3101-01	644.41	J0850	per vial
Cytoxan® Lyophilized					
Cyclophosphamide, lyophilized	100 mg	00015-0539-41	6.45	J9093	per 100 mg
	200 mg	00015-0546-41	12.25	J9094	per 200 mg
	500 mg	00015-0547-41	25.71	J9095	per 500 mg
	1 g	00015-0548-41	51.43	J9096	per 1 g
	2 g	00015-0549-41	102.89	J9097	per 2 g
Cytoxan® Tablets					
Cyclophosphamide, tablets, 25 mg	100 per bottle	00015-0504-01	222.95	J8530	25 mg
Cyclophosphamide, tablets, 50 mg	100 per bottle	00015-0503-01	409.16	J8530	25 mg
Cyclophosphamide, tablets, 50 mg	1,000 per bottle	00015-0503-02	3,897.01	J8530	25 mg
Cytarabine, pwd	100 mg	55390-0131-10	6.25	J9100	per 100 mg
	500 mg	55390-0132-10	25.00	J9110	per 500 mg
	1 g	55390-0133-01	50.00	J9110	per 500 mg
	2 g	55390-0134-01	98.90	J9110	per 500 mg
DTIC-Dome®					
Dacarbazine, pwd	200 mg	00026-8151-20	26.61	J9140	per 200 mg
DaunoXome®					
Daunorubicin citrate liposome inj. (2 mg/mL)	50 mg	56146-0301-01	340.00	J9151	per 10 mg
Cerubidine®					
Daunorubicin HCl, pwd	20 mg	55390-0281-10	168.50	J9150	per 10 mg
DDAVP®					
Desmopressin Acetate, sol (4 mcg/mL)	1 mL	00075-2451-01	26.67	J2597	per 4 mcg
Zinecard®					
Dexrazoxane for injection	250 mg	00013-8715-62	158.49	J1190	per 250 mg
	500 mg	00013-8725-89	316.95	J1190	per 250 mg
Diphenhydramine HCl, sol (50 mg/1 mL)	50 mg	00641-0376-25	1.24	J1200	
Taxotere®					
Docetaxel for injection	20 mg	00075-8001-20	284.36	J9170	per 20 mg
	80 mg	00075-8001-80	1,137.43	J9170	per 20 mg
Anzemet®					
Dolasetron mesylate, sol (20 mg/mL)	5 mL	00088-1206-32	155.88	J1260	per 1 mg
Rubex®					
Doxorubicin, pwd	50 mg	00015-3352-22	197.15	J9000	per 10 mg
	100 mg	00015-3353-22	394.29	J9000	per 10 mg
Bedford Laboratories					
Doxorubicin, pwd	10 mg	55390-0231-10	45.08	J9000	per 10 mg
	20 mg	55390-0232-10	90.16	J9000	per 10 mg
	50 mg	55390-0233-01	225.40	J9000	per 10 mg

ONCOLOGY THERAPEUTICS NETWORK

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	NOV AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Doxorubicin, sol (2 mg/mL)	10 mg	55390-0235-10	47.35	J9000	per 10 mg
	20 mg	55390-0236-10	94.70	J9000	per 10 mg
	50 mg	55390-0237-01	236.74	J9000	per 10 mg
	200 mg MDV	55390-0238-01	945.98	J9000	per 10 mg
Adriamycin PFS™ Doxorubicin, RDF pwd	10 mg	00013-1086-91	53.64	J9000	per 10 mg
	50 mg	00013-1106-79	268.18	J9000	per 10 mg
	150 mg MDV	00013-1116-83	788.44	J9000	per 10 mg
Doxorubicin, pfs sol (2 mg/mL)	10 mg	00013-1136-91	56.34	J9000	per 10 mg
	20 mg	00013-1146-94	112.66	J9000	per 10 mg
	50 mg	00013-1156-79	281.68	J9000	per 10 mg
	75 mg	00013-1176-87	422.51	J9000	per 10 mg
	200 mg MDV	00013-1166-83	1,104.13	J9000	per 10 mg
DOXIL® Doxorubicin, HCl liposome inj. (2mg/mL)	20 mg	61471-0295-12	656.25	J9999*	
Procrit® Epoetin alfa	2,000 units/ mL	59676-0302-01	24.00	Q0136†	1,000 units
	3,000 units/ mL	59676-0303-01	36.00	Q0136†	1,000 units
	4,000 units/ mL	59676-0304-01	48.00	Q0136†	1,000 units
	10,000 units/ mL	59676-0310-01	120.00	Q0136†	1,000 units
	20,000 units/ 1 mL MDV	59676-0320-01	240.00	Q0136†	1,000 units
	40,000 units/ 1 mL SDV	59676-0340-01	480.00	Q0136†	1,000 units
VePesid® Capsules - Etoposide, capsules, 50 mg	20 per box	00015-3091-45	967.34	J8560	50 mg
VePesid® For Injection Etoposide, injection (20 mg/mL)	100 mg MDV	00015-3095-20	136.49	J9182	per 100 mg
	150 mg MDV	00015-3084-20	204.74	J9182	per 100 mg
	500 mg MDV	00015-3061-20	665.38	J9182	per 100 mg
	1 gm MDV	00015-3062-20	1,296.64	J9182	per 100 mg
Etopophos® - Etoposide phosphate for injection	100 mg	00015-3404-20	124.14	J9182	per 100 mg
Fludara® Fludarabine phosphate, pwd	50 mg	50419-0511-06	242.25	J9185	per 50 mg
Fluorouracil, sol (50 mg/mL)	500 mg	00013-1036-91	3.20	J9190	per 500 mg
	2,500 mg	00013-1046-94	16.04	J9190	per 500 mg
	5,000 mg	00013-1056-94	32.06	J9190	per 500 mg
Neupogen® G-CSF (Filgrastim), sol (0.3 mg/mL)	300 mcg	55513-0530-10	165.30	J1440	per 300 mcg
	480 mcg	55513-0546-10	274.40	J1441	per 480 mcg
Gemzar® Gemcitabine HCl	200 mg	00002-7501-01	93.12	J9201	per 200 mg
	1 g	00002-7502-01	465.59	J9201	per 200 mg
Leukine® - GM-CSF (Sargramostim), lyophilized	250 mcg	58406-0002-33	134.85	J2820	per 50 mcg
Leukine Liquid® (Sargramostim), solution	500 mcg	58406-0001-35	252.06	J2820	per 50 mcg
Zoladex® Goserelin acetate, implant	3.6 mg syringe	00310-0960-36	469.99	J9202	per 3.6 mg
	10.8 mg syringe	00310-0961-30	1,409.98	J9202	per 3.6 mg
Kytril® Granisetron HCl, sol (1 mg/mL)	1 mL	00029-4149-01	195.20	J1626	per 100 mcg
	4 mL	00029-4152-01	780.80	J1626	per 100 mcg
Ifex® Ifosfamide	1 g	00015-0556-41	141.76	J9208	per 1 g
	3 g	00015-0557-41	425.29	J9208	per 1 g
Ifex®/Mesnex™ - Ifosfamide (10 x 1 g)/mesna (10 x 1 g MDV)	Combo-Pack	00015-3554-27	2,474.09	J9208/J9209	
- Ifosfamide (2 x 3 g)/mesna (6 x 1 g MDV)	Combo-Pack	00015-3564-15	1,484.39	J9208/J9209	
- Ifosfamide (5 x 1 g)/mesna (3 x 1 g MDV)	Combo-Pack	00015-3556-26	1,023.90	J9208/J9209	
Venoglobulin S Immune globulin intravenous, 5% sol w/IV set	2.5 g	49669-1612-01	225.00	J1561	per 500 mg
	5 g	49669-1613-01	450.00	J1561	per 500 mg
	10 g	49669-1614-01	900.00	J1561	per 500 mg
Immune globulin intravenous, 10% sol w/IV set	5 g	49669-1622-01	475.00	J1562	per 5 g
	10 g	49669-1623-01	950.00	J1562	per 5 g
	20 g	49669-1624-01	1,900.00	J1562	per 5 g
Immune globulin intravenous, 10% sol w/IV set	1 g	00026-0648-12	90.00		
	5 g	00026-0648-20	450.00		
	10 g	00026-0648-71	900.00		
	20 g	00026-0648-24	1,800.00		

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	NOV AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Immune globulin intravenous, 5%-10% w/IV set	2.5 g	52769-0471-72	223.75	J1561 or J1562	
	5 g	52769-0471-75	447.50	J1561 or J1562	
	10 g	52769-0471-80	895.00	J1561 or J1562	
Rho D immune globulin intravenous	120 mcg	60492-0021-01	142.00	J2792	
	300 mcg	60492-0023-01	324.50	J2792	
	1,000 mcg	60492-0024-01	1,081.50	J2792	
Intron® A					
Interferon alfa-2b, solution HSA-free	3 MIU	00085-1184-01	35.63	J9214	per 1 MIU
	3 MIU PAK	00085-1184-02	35.63	J9214	per 1 MIU
	5 MIU	00085-1191-01	59.38	J9214	per 1 MIU
	5 MIU PAK	00085-1191-02	59.38	J9214	per 1 MIU
	10 MIU	00085-1179-01	118.76	J9214	per 1 MIU
	10 MIU PAK	00085-1179-02	118.76	J9214	per 1 MIU
	18 MIU MDV	00085-1168-01	213.77	J9214	per 1 MIU
	25 MIU MDV	00085-1133-01	296.93	J9214	per 1 MIU
Interferon alfa-2b, pwd	3 MIU MDV	00085-0647-03	35.63	J9214	per 1 MIU
	5 MIU MDV	00085-0120-02	59.38	J9214	per 1 MIU
	10 MIU MDV	00085-0571-02	118.76	J9214	per 1 MIU
	18 MIU MDV	00085-1110-01	213.77	J9214	per 1 MIU
	25 MIU MDV	00085-0285-02	296.93	J9214	per 1 MIU
	50 MIU MDV	00085-0539-01	593.81	J9214	per 1 MIU
Roferon® A					
Interferon alfa 2a, pwd w/3 mL diluent	18 MIU	00004-1993-09	203.48	J9213	per 3 MIU
Interferon alfa 2a, sol (3 MIU/mL)	3 MIU	00004-2009-09	34.97	J9213	per 3 MIU
Interferon alfa 2a, sol (6 MIU/mL)	6 MIU	00004-2007-09	69.91	J9213	per 3 MIU
Interferon alfa 2a, sol (10 MIU/mL)	9 MIU	00004-2010-09	98.44	J9213	per 3 MIU
Interferon alfa 2a, sol (6 MIU/mL)	18 MIU	00004-2011-09	209.60	J9213	per 3 MIU
Interferon alfa 2a, sol (36 MIU/mL)	36 MIU	00004-2012-09	419.26	J9213	per 3 MIU
Camptosar®					
Irinotecan HCl injection, CPT-11 (20 mg/mL)	2 mL	00009-7529-02	231.80	J9206	per 20 mg
	5 mL	00009-7529-01	579.53	J9206	per 20 mg
Leucovorin, pwd	50 mg	55390-0051-10	18.44	J0640	per 50 mg
	100 mg	55390-0052-10	35.00	J0640	per 50 mg
	200 mg	55390-0053-01	78.00	J0640	per 50 mg
	350 mg	58406-0623-07	137.94	J0640	per 50 mg
Lupron®					
Leuprolide acetate depot susp. (7.5 mg/mL)	7.5 mg	00300-3629-01	594.65	J9217	per 7.5 mg
	22.5 mg	00300-3346-01	1,783.95	J9217	per 7.5 mg
Lorazepam, sol (2 mg/mL)	2 mg MDV	00008-0581-04	9.85	J2060	per 2 mg
Lorazepam, sol (2 mg/mL)	20 mg MDV	00008-0581-01	87.74	J2060	per 2 mg
Lorazepam, sol (4 mg/mL)	40 mg MDV	00008-0570-01	109.66	J2060	per 2 mg
Lorazepam, sol (2 mg/mL), w/ syringe	2 mg	00008-0581-02	10.39	J2060	per 2 mg
Mannitol, 25% sol	50 mL	00074-4031-01	1.93	J2150	per 50 mL
Mustargen®					
Mechlorethamine HCl, pwd	10 mg	00006-7753-31	11.22	J9230	per 10 mg
Megace®					
Megestrol acetate, tablets, 20 mg	100 per bottle	00015-0595-01	75.68		
Megestrol acetate, tablets, 40 mg	100 per bottle	00015-0596-41	134.96		
	250 per bottle	00015-0596-46	330.68		
	500 per bottle	00015-0596-45	647.88		
Megace® Oral Suspension					
Megestrol acetate, oral suspension	8 fl oz	00015-0508-42	137.24		
Alkeran®					
• Melphalan hydrochloride, pwd	50 mg	00173-0130-93	382.61	J9245	per 50 mg
• Melphalan hydrochloride, tablets, 2 mg	50 per bottle	00173-0045-35	109.21	J8600	2 mg
Mesnex™					
• Mesna, sol (100 mg/mL)	10 mL	00015-3563-02	192.16	J9209	per 200 mg
Methotrexate, pwd	20 mg	58406-0673-01	5.03	J9250	per 5 mg
	1,000 mg	58406-0671-05	61.44	J9260	per 50 mg
Methotrexate, pres. free sol (25 mg/mL)	50 mg	55390-0031-10	6.88	J9260	per 50 mg
	100 mg	55390-0032-10	8.75	J9260	per 50 mg
	200 mg	55390-0033-10	17.50	J9260	per 50 mg
	250 mg	55390-0034-10	26.88	J9260	per 50 mg
Methotrexate, sol w/pres. (25 mg/mL)	50 mg	58406-0681-14	4.75	J9260	per 50 mg
	250 mg	58406-0681-17	20.48	J9260	per 50 mg
Methotrexate, tablets, 2.5 mg	100 per bottle	00555-0572-02	362.95	J8610	2.5 mg
	36 per bottle	00555-0572-35	130.05	J8610	2.5 mg
Mutamycin®					
Mitomycin, pwd	5 mg	00015-3001-20	134.11	J9280	per 5 mg
	20 mg	00015-3002-20	452.91	J9290	per 20 mg
	40 mg	00015-3059-20	915.09	J9291	per 40 mg

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC	NOV AWP/VIAL	'99 HCPCS CODE	BILLING UNITS
Novantrone®					
Mitoxantrone, sol (2 mg/mL)	20 mg MDV	58406-0640-03	885.89	J9293	per 5 mg
	25 mg MDV	58406-0640-05	1,107.33	J9293	per 5 mg
	30 mg MDV	58406-0640-07	1,328.83	J9293	per 5 mg
Sandostatin®					
Octreotide Acetate, sol (50 mcg/mL)	50 mcg amp	00078-0180-03	6.07	J9999*/J3490†	
Octreotide Acetate, sol (100 mcg/mL)	100 mcg amp	00078-0181-03	11.77	J9999*/J3490†	
Octreotide Acetate, sol (500 mcg/mL)	500 mcg amp	00078-0182-03	56.80	J9999*/J3490†	
Sandostatin LAR® Depot					
Octreotide Acetate, inj	10 mg	00078-0340-84	1,368.75	J9999*/J3490†	
Octreotide Acetate, inj	20 mg	00078-0341-84	1,368.75	J9999*/J3490†	
Octreotide Acetate, inj	30 mg	00078-0342-84	2,053.12	J9999*/J3490†	
Zofran®					
Ondansetron HCl, sol (2 mg/mL)	40 mg MDV	00173-0442-00	244.43	J2405	per 1 mg
Ondansetron HCl, sol (2 mg/mL)	4 mg	00173-0442-02	24.45	J2405	per 1 mg
Ondansetron HCl, sol premixed (32 mg/50 mL D5W)	32 mg bag	00173-0461-00	206.41	J2405†	per 1 mg
Neumega®					
Oprelvekin	5 mg	58394-004-01	248.75	J2355	per 5 mg
TAXOL®					
Paclitaxel, semi-synthetic sol (6mg/ml)	30 mg	00015-3475-30	182.63	J9265	per 30 mg
	100 mg	00015-3476-30	608.76	J9265	per 30 mg
	300 mg	00015-3479-11	1,826.25	J9265	per 30 mg
Aredia®					
Pamidronate disodium, pwd	30 mg	00083-2601-04	244.75	J2430	per 30 mg
	90 mg	00083-2609-01	678.31	J2430	per 30 mg
Nipent™					
Pentostatin, pwd	10 mg	62701-0800-01	1,645.00	J9268	per 10 mg
Prochlorperazine, sol (5 mg/mL)	10 mL vial	00007-3343-01	41.00	J0780	
Prochlorperazine, tablets, 10 mg	100 per box	00007-3367-20	94.50	J0780	
Zantac®					
Ranitidine, sol (50 mg/2 mL)	2 mL	00173-0362-38	3.99	J9999*/J3490†	
Respigam®					
Respiratory syncitial virus immune globulin, human	20 mL	60574-2102-01	427.82	J1565	per 50 mg
	50 mL	60574-2101-01	717.57	J1565	per 50 mg
Rituxan™					
Rituximab	100 mg	50242-0051-21	442.41	J9310	per 100 mg
Zanosar®					
Streptozocin, pwd	1 g	00009-0844-01	114.65	J9320	per 1 g
Vumon®					
Teniposide, 50 mg	5 mL amp	00015-3075-19	195.78	J9999*	per 50 mg
Thioplex®					
Thiotepa, pwd	15 mg	58406-0661-02	105.58	J9340	per 15 mg
Hycamtin™					
Topotecan HCl lyoph pwd	4 mg	00007-4201-01	603.95	J9350	per 4 mg
	4 mg, 5s	00007-4201-05	603.95	J9350	per 4 mg
Herceptin®					
Trastuzumab	440 mg	50242-0134-60	2,262.50	J9999*/J3490†	
Neutrexin®					
Trimetrexate glucuronate, pwd	25 mg, 10s ea.	58178-0020-10	735.00	J3305	per 25 mg
	25 mg, 50s ea.	58178-0020-50	3,675.00	J3305	per 25 mg
Trimetrexate glucuronate, sol	200 mg	58178-0021-01	588.05	J3305	per 25 mg
Urokinase, sol (5,000 IU/mL)	5,000 IU	00074-6111-01	59.59	J3364	per 5,000 IU
	9,000 IU	00074-6145-02	103.91	J3364	per 5,000 IU
Vinblastine sulfate, pwd	10 mg	55390-0091-10	21.25	J9360	per 1 mg
Vinblastine sulfate, sol (1 mg/mL)	10 mg	63323-0278-10	43.23	J9360	per 1 mg
Vincristine, preservative free sol (1 mg/mL)	1 mg	00013-7456-86	43.23	J9370	per 1 mg
	1 mg	61703-0309-06	31.75	J9370	per 1 mg
	2 mg	00013-7466-86	86.46	J9375	per 2 mg
	2 mg	61703-0309-16	38.25	J9375	per 2 mg
Vincristine, preservative free sol (5 mg/mL)	50 mg	61703-0210-11	7.47	J9380	per 5 mg
	150 mg	61703-0210-31	20.31	J9380	per 5 mg
NAVELBINE®					
Vinorelbine tartrate, sol (10 mg/mL)	1 mL	00173-0656-01	79.48	J9390	per 10 mg
	5 mL	00173-0656-44	397.38	J9390	per 10 mg

- An AWP, HCPCS code or NDC that has changed or been added has been highlighted in color.
* The drug code J9999 is defined as "not otherwise classified, antineoplastic drug." The Health Care Financing Administration (HCFA) has not assigned specific codes to these drugs.
† The drug code J3490 is defined as "unclassified drug." These drugs may or may not be defined as an unclassified drug in your area. Consult your local carrier for the appropriate code.
‡ Q0136 is the code for non-ESRD (End Stage Renal Disease) use.
+ J2405 should be used for all formulations of Zofran.